US Environmental Protection Agency
Office of Pesticide Programs

Petition for Cyazofamid

April 2014

APPLICATION FOR EXTENSION OF EXCLUSIVE USE PERIOD FOR CYAZOFAMID

DATA SUPPORTING THE REGISTRATIONS OF

CYAZOFAMID TECHNICAL (EPA REGISTRATION NUMBER 71512-2)

RANMAN 400SC (EPA REGISTRATION NUMBER 71512-3)

SUPPORTING MINOR CROPS:

CROP GROUP 5 (BRASSICA (COLE) LEAFY VEGETABLES)

CROP GROUP 8 (FRUITING VEGETABLES) AND OKRA

CROP GROUP 9 (CUCURBITS VEGETABLES)

CARROT

GRAPES (EAST OF ROCKY MOUNTAINS)

TOMATO (GREENHOUSE TRANSPLANT)

SPINACH

HOP

AUTHORS

Melvin D. Grove, Ph.D., Gregory A. Leyes, Ph.D.,
Noriko Nakada, Max Parks, Michael A. Peplowski

SUBMITTER

ISK Biosciences Corporation
7470 Auburn Road, Suite A
Concord, OH 44077

DATE

SEPTEMBER 4, 2013

STATEMENT OF NO CLAIM OF CONFIDENTIALITY*

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that information not designated as within the scope of FIFRA sec. 10(d)(1)(A), (B), or (C) and which pertains to a registered or previously registered pesticide is not entitled to confidential treatment and may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRA 10(g).

COMPANY: ISHIHARA SANGYO KAISHA, LTD.

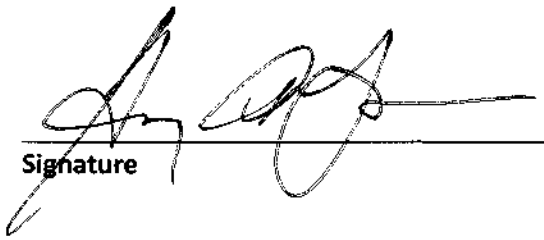
COMPANY AGENT:
(Submitter)

Gregory A. Leyes

Typed Name

Agent for ISHIHARA SANGYO KAISHA, LTD.
Vice President, Regulatory Affairs
ISK Biosciences Corporation

Title



Signature

September 5, 2013

Date

* We submitted this material to the United States Environmental Protection Agency specifically under provisions contained in FIFRA as amended, and thereby consent to use and disclosure of this material by EPA according to FIFRA. Notwithstanding the wording of our marking (either as "Property of ISK BIOSCIENCES CORPORATION" or "Property of ISHIHARA SANGYO KAISHA, LTD."), this marking by itself conveys no supplemental claims of confidentiality under FIFRA Sections 10(a) or 10(b). In submitting this material to the EPA according to the method and format requirements contained in PR Notice 86-5 and PR Notice 2011-3, we do not waive any protection or right involving this material that would have been claimed by ISK BIOSCIENCES CORPORATION or by ISHIHARA SANGYO KAISHA, LTD. or agents of these companies anywhere else in the world, if this material had not been submitted to the EPA.

COMPLIANCE STATEMENT

ISK Biosciences Corporation

This report is a compilation of information and is not subject to the principles of Good Laboratory Practice Regulations set forth in Title 40, Part 160 of the Code of Federal Regulations of the United States of America.

Author
Noriko Nakada
ISK BIOSCIENCES CORPORATION

Sept. 4, 2013
Date

Gregory A. Leyes
Vice President, Regulatory Affairs
ISK BIOSCIENCES CORPORATION
Agent for STUDY SPONSOR
ISHIHARA SANGYO KAISHA, LTD.

September 5, 2013
Date

Michael A. Peplowski
Manager, Product Registrations & Quality Assurance, Regulatory Affairs
ISK BIOSCIENCES CORPORATION, APPLICANT

September 5, 2013
Date

TABLE OF CONTENTS

TABLE OF CONTENTS - CONTINUED

LIST OF ABBREVIATIONS

CAA: Carboxylic Acid Amides

EPA: United States Environmental Protection Agency

FRAC: Fungicide Resistance Action Committee

IPM: Integrated Pest Management

PA: Phenylamides

PMSP: Pest Management Strategic Plans

QoI: Quinone Outside Inhibitors

NASS: National Agricultural Statistics Program

USDA: United States Department of Agriculture

APPLICATION FOR EXTENSION OF EXCLUSIVE USE PERIOD FOR CYAZOFAMID DATA SUPPORTING THE REGISTRATION OF CYAZOFAMID TECHNICAL (EPA REG. NO. 71512-2), AND RANMAN 400SC (EPA REG. NO. 71512-3), A CYAZOFAMID-CONTAINING END-USE PRODUCT

PURPOSE

The purpose of this submission is to support the request of ISK Biosciences Corporation (ISKBC) for the US Environmental Protection Agency (EPA or the Agency) to extend the exclusive use period for Cyazofamid data for an additional three years. This request for a three-year extension is based on the facts that Cyazofamid is registered and marketed for use on more than nine minor crops, these uses were registered within the required time period, and the registered uses meet one or more of the four criteria necessary to support the request.

INTRODUCTION AND BACKGROUND

The 1996 Food Quality Protection Act (FQPA) amendments to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provide additional exclusive use data protection for minor use registrations. FIFRA defines minor use as a use on a crop with acreage of less than 300,000 acres or, in the alternative, when EPA and the US Department of Agriculture (USDA) determine that a use does not provide sufficient economic incentive to support the registration of a pesticide for such use. If EPA determines that one of four statutory criteria below are met by the minor use registrations, the period for exclusive use data protection can be extended one year for every three minor uses registered during the first seven years of the original registration. The maximum time period that the exclusive use period can be extended is three years. The four criteria for extension of the exclusive use period in FIFRA Sec. 3(c)(1)(F)(ii) are:

> (I) there are insufficient efficacious alternative registered pesticides available for the use;
> (II) the alternatives to the minor use pesticide pose greater risks to the environment or human health;
> (III) the minor use pesticide plays or will play a significant part in managing pest resistance; or
> (IV) the minor use pesticides plays or will play a significant part in an integrated pest management program.

Before EPA considers any request to extend an exclusive use period, the Agency must determine that there are, in fact, data entitled to exclusive use. FIFRA and its supporting regulations define data that are entitled to exclusive use protection. Briefly, exclusive use data are: (1) data that pertain to a new active ingredient (or new combination of active ingredients) initially registered after September 30, 1978; (2) the data must have been submitted in support of the first registration of the new active ingredient or an amendment to add a new use to the initial registration; and (3) the data must not have been submitted to satisfy a requirement under Section 3(c)(2)(B) of FIFRA.

EPA granted the initial registration for the RANMAN 400SC end use product (EPA Reg. No. 71512-3) containing Cyazofamid on November 12, 2004 and for Technical Cyazofamid (EPA Reg. No. 71512-2) on November 9, 2004. The initial registration included Cucurbit Vegetables (Crop Group 9); and potatoes and field tomatoes. Potatoes and tomatoes are not part of the submission supporting the requested exclusive use period extension. On August 1, 2008, EPA amended the RANMAN 400SC registration to add Carrot. On July 29, 2009, EPA amended the RANMAN 400SC registration to add Grapes, East of the Rocky Mountains; and Fruiting Vegetables (Crop Group 8) and Okra. Further, on August 13, 2010, EPA amended the RANMAN 400SC registration to add Brassica (Cole) Leafy Vegetables (Crop Group 5) and Turnip Greens; Spinach; and Hops.[1] Note that these uses were registered within seven years of the initial Cyazofamid registration. Minor uses included in the 2004, 2008, 2009 and 2010 registration actions are thus eligible for consideration in a request to extend the exclusive use period. On September 14, 2012, EPA further amended the RANMAN 400SC registration to add basil; succulent-podded and succulent-shelled beans; and expanded label from spinach to leafy greens (Crop Subgroup 4A) including lettuce; and expanded from potatoes to tuberous and corm vegetables (Crop Subgroup 1C) and expanded fruiting vegetables crop Group 8 to Group 8-10. However, the crops added in September 14, 2012 amendment are not within the scope of this requested extension of the exclusive use period as the amendment was not within 7 years of the initial Cyazofamid registration. We will discuss below the minor crop qualification for extension of the exclusive use period with the crops registered within the qualified registration period of 7 years from the initial Cyazofamid registration.

Based on these registrations and the data ISKBC submitted to support the registrations, EPA can conclude that there are data supporting the registration of a new active ingredient first registered after September 30, 1978 entitled to exclusive use protection. The exclusive use period for Cyazofamid data currently exists until November 9, 2014. This submission requests that the exclusive use period be extended through November 9, 2017.

For EPA to grant the requested extension of the exclusive use period, ISKBC must further demonstrate that the uses registered in 2004, 2008, 2009 and 2010 include the number of minor crops necessary for the extension, and that the registration of Cyazofamid for use on these minor crops meets one of the required statutory criteria needed to support the extension of the exclusive use period. The remainder of this submission documents that the conditions for extending exclusive use have been met.

Profile for Cyazofamid

Cyazofamid is a unique, locally systemic fungicide from a new class of chemistry, the cyanoimidazoles, and is active at low seasonal use rates for control of late blight, Phytophthora blight, downy mildews, clubroot, *Pythium* spp. and white rust in several vegetables, potatoes, carrots, grapes and hops. Cyazofamid has been proven to kill Oomycete fungi by respiratory inhibition, specifically at Complex III in the mitochondria of Oomycete fungi. Cyazofamid inhibits Qi (ubiquinone-reducing site) of Complex III of the said fungi, which has only been reported for one other fungicide (amisulbrom) which is not registered in the U.S. The unique mode of action of Cyazofamid on these fungi makes Cyazofamid

[1] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Issuance and Amendments Accepted Dated: November 12, 2004, August 1, 2008, July 29, 2009 and August 13, 2010." Environmental Protection Agency, Washington, DC.

particularly useful for resistance management to alternate or combine with application of several other "single-site" fungicides, such as cymoxanil, mandipropamid, fluopicolide, propamocarb HCl, mefenoxam and dimethomorph which have been registered for use for control of these diseases. This high level of efficacy and significantly lower seasonal application rate will lead to replacement of older, high use rate fungicides (such as chlorothalonil, maneb, mancozeb, etc.). Cyazofamid also effectively prevents infection from Oomycete diseases to the crops listed above and leaves low residue on the crop at harvest.

The commercial label for an end-use product containing Cyazofamid (i.e., EPA Reg. No. 71512-3-279) includes resistance management labeling in the directions for use section of the label as recommended by Pesticide Registration (PR) Notice 2001-5 "Guidance for Pesticide Registrants on Pesticide Resistance Management Labeling." PR Notice 2001-5 language is most relevant to fungicides that are prone to developing resistance. Fungicide Resistance Action Committee (FRAC) lists Cyazofamid as "Resistance risk unknown but assumed to be medium to high (mutations at target site known in model organisms)" and indicated "Resistance management required." Preventing resistance is important to ISK, and the resistance language tailored to Cyazofamid is on the label below. In addition, Cyazofamid is an excellent fit with many Integrated Pest Management (IPM) programs and therefore the IPM language for Cyazofamid is given below as well.

GROUP	21	FUNGICIDE

RESISTANCE MANAGEMENT

Some plant pathogens are known to develop resistance to products used repeatedly for disease control. RANMAN 400SC's mode/target site of action is complex III of fungal respiration: ubiquinone reductase, Qi site, FRAC code 21. A disease management program that includes alternation or tank mixes between RANMAN 400SC and other labeled fungicides that have a different mode of action and/or control pathogens not controlled by RANMAN 400SC is essential to prevent disease resistant pathogens populations from developing. RANMAN 400SC should not be utilized continuously nor tank mixed with fungicides that have shown to have developed fungal resistance to the target disease.

Since pathogens differ in their potential to develop resistance to fungicides, follow the directions outlined in the "Directions For Use" section of this label for specific resistance management strategies for each crop. Consult with your Federal or State Cooperative Extension Service representatives for guidance on the proper use of RANMAN 400SC in programs that seek to minimize the occurrence of disease

INTEGRATED PEST MANAGEMENT

RANMAN 400SC is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. Although RANMAN 400SC has limited systemic activity, it should be utilized as a protectant fungicide and applied before the disease infects the crop. Depending upon the level of disease pressure, good protection of the crop against disease can be expected over a period of 7 to 10 days. RANMAN 400SC is recommended for use as part of an Integrated Pest Management (IPM) program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage. Practices known to reduce disease development should be followed. Consult your state cooperative extension service or local agricultural authorities for additional IPM strategies established in your area. RANMAN 400SC may be used in State Agricultural Extension advisory (disease forecasting) programs that recommend application timing based upon environmental factors that favor disease development.

RATIONALE AND DISCUSSION SUPPORTING THE EXTENSION REQUEST

1. Minor Uses for Consideration

As stated earlier, EPA registered multiple uses for Cyazofamid on November 12, 2004, followed by additional crop registrations in August 1, 2008, July 29, 2009, August 13, 2010 and September 14, 2012, although the crops added in September 14, 2012 amendment are not within a scope of this requested extension of the exclusive use period as the amendment was not within 7 years of the initial Cyazofamid registration. A copy of the latest EPA-stamped label (i.e., EPA Reg. No. 71512-3) is provided as Appendix 1. FMC Corporation distributes Cyazofamid 400SC for ISKBC. FMC holds a supplemental registration for RANMAN 400SC (i.e., EPA Reg. No. 71512-3-279). A copy of the current commercial label is provided as Appendix 2[2]; the label demonstrates that ISKBC through FMC is marketing Cyazofamid for each of the uses approved by EPA in 2004, 2008, 2009, 2010 and 2012.

ISKBC has verified that 48 crops, specifically in the following crops, meet the less than 300,000 acre criterion and within 7 years period from the initial Cyazofamid registration for classification as a minor use:

- 18 minor crops listed in Crop Group 5: Brassica (Cole) Leafy Vegetables, including Turnip Greens (Crop Group 2)
- 11 minor crops listed in Crop Group 8 (Fruiting Vegetables and Okra
- 14 minor crops listed in Crop Group 9: Cucurbit Vegetables
- Carrot
- Grape, East of the Rocky Mountains
- Tomato, Greenhouse Transplant
- Spinach
- Hop

ISKBC examined the USDA National Agricultural Statistics Service (NASS) and the OPPTS Guideline 860.1500 Crop Field Trials to determine the total acreage of all the target crops planted in the United States.[3, 4] The NASS data is based on the 2007 Census of Agriculture. The information from these sources is summarized by crop in the discussion sections for each respective crop or crop group. For crops where there was available data, the major/minor status was verified. Crops not individually surveyed in the U.S. Census of Agriculture were assumed to be below the 300,000 acre threshold, and therefore considered minor crops.

[2] This label was the most recent label in the marketplace prior to the newest EPA-approved label (i.e., 10/01/12). (Appendix 2)
[3] United States, Environmental Protection Agency. Prevention, Pesticides and Toxic Substances. *Residue Chemistry Test Guidelines OCSPP 860.1500 Crop Field Trials.* Pages 60-62. EPA, August 1996.
[4] 2007 Census of Agriculture. United States Department of Agriculture, National Agricultural Statistics Service. http://www.agcensus.usda.gov/Publications/2007/Full_Report/usv1.pdf

2. Alternative Fungicides Considered

Method for determining Alternative Fungicides

In order to determine the alternative fungicides used on these crops for the target pathogens, competitor products and labels were evaluated. Sulfur, fumigant, petroleum oil and biological products were excluded as they were not considered to be viable products based on efficacy or market penetration, while the remaining products were considered viable alternatives. In addition, to confirm the competitor products, data from GfK Kynetec[5] were reviewed for as many crops as were available in the database. Based on this research, the alternative fungicides were divided by crop group and by pathogen, and are listed in Tables 2A through 2H. A brief discussion for each alternative fungicide is also included. It must be noted that a distinction was made between fungicides registered for use on various crops for various target pathogens, and fungicides actually labeled for use on these crops and pathogens. This distinction was made because, although many fungicides may be registered for specific use sites, they may not currently be labeled and marketed for those use sites. Many of the documents used to support this petition refer to and discuss as alternatives fungicides that have been registered with EPA, but ISK does not believe these can be considered viable alternatives if they are not currently used or available on the market.

Alternative Fungicides (active ingredients) by Use Sites, Target Pathogens, and FRAC Category

TABLE 2A: CROP GROUP 5 (BRASSICA (COLE) LEAFY VEGETABLES) ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Clubroot (*Plasmodiophora brassicae*)	Fluazinam	29
Downy mildew (*Peronospora parasitica*)	Mefenoxam	4
	Fenamidone	11
	Phosphoric Acid	33
	Dimethomorph	40
	Mandipropamid	40
	Maneb	M3
	Chlorothalonil	M5

[5] GfK Kynetec, St. Louise, MO.

TABLE 2B: CROP GROUP 8 (FRUITING VEGETABLES) AND OKRA ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Late blight (*Phytophthora infestans*)	Fenamidone	11
	Famoxadone+Cymoxanil	11/27
	Fluopicolide	43
	Cuprous Oxide	M1
	Copper Hydroxide	M1
	Copper Sulfate	M1
	Copper Oxychlorides	M1
Phytophthora blight (*Phytophthora capsici*)	Fenamidone	11
	Famoxadone+Cymoxanil	11/27
	Mandipropamid	40
	Fluopicolide	43
	Copper	M1
	Maneb	M3

TABLE 2C: CROP GROUP 9 (CUCURBITS VEGETABLES) ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Downy mildew (*Pseudoperonospora cubensis*),	Fenamidone	11
	Famoxadone+Cymoxanil	11/27
	Zoxamide	22
	Cymoxanil	27
	Propamocarb HCl	28
	Fosetyl-Al	33
	Phosphoric Acid	33
	Dimethomorph	40
	Fluopicolide	43
	Copper	M1
	Copper Hydroxides	M1
	Cuprous Oxide	M1
	Cuprous Oxychloride	M1
	Copper Sulfate	M1
	Mancozeb	M3
	Maneb	M3
	Chlorothalonil	M5

TABLE 2C: CROP GROUP 9 (CUCURBITS VEGETABLES) ALTERNATIVE FUNGICIDES - CONTINUED

Pathogen	Active Ingredients	FRAC Category
Phytophthora blight (*Phytophthora capsici*)	Mefenoxam	4
	Famoxadone	11
	Cymoxanil	27
	Phosphorous Acid	33
	Dimethomorph	40
	Mandipropamid	40
	Fluopicolide	43

TABLE 2D: CARROT ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Cavity Spot (*Pythium ultimum*)	Mefenoxam	4
	Fenamidone	11
Root Dieback (*P. violae, P. sulcatum*)	Mefenoxam	4
Forking (*P. Irregulate, P. splendens*)	Mefenoxam	4

TABLE 2E: GRAPE, EAST OF THE ROCKY MOUNTAINS, ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Downy mildew (*Plasmopara viticola*)	Fenamidone	11
	Famoxadone+Cymoxanil	11/27
	Phosphorous Acid	33
	Mandipropamid	40
	Fluopicolide	43
	Copper Oxychlorides	M1
	Copper Sulfate	M1
	Mancozeb	M3
	Ziram	M3

TABLE 2F: TOMATO GREENHOUSE TRANSPLANT ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Pythium Damping-off (*Pythium* spp.)	Mefenoxam	4
	Propamocarb HCl	28
	Fosetyl-Al	33

TABLE 2G: SPINACH ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
White rust (*Albugo occidentalis)*	Mefenoxam	4
	Azoxystrobin	11
	Fenamidone	11
	Pyraclostrobin	11
	Famoxadone/Cymoxanil	11/27
	Fosetyl-Al	33
	Copper Hydroxide	M1

TABLE 2H: HOP ALTERNATIVE FUNGICIDES

Pathogen	Active Ingredients	FRAC Category
Downy mildew (*Pseudoperonospora humuli*)	Mefenoxam	4
	Metalaxyl	4
	Famoxadone/Cymoxanil	11/27
	Cymoxanil	27
	Fosetyl-Al	33
	Phosphorous Acid	33
	Dimethomorph	40
	Mandipropamid	40
	Copper Sulfate, Copper Oxide	M1
	Folpet	M4

Alternative Fungicide Profiles

The different use sites and target pathogens of Cyazofamid can be treated (in most cases) with many common fungicides and classes of fungicides. Below are brief profiles of the different compounds organized by mode of action and chemical class. This information is provided as general background information on resistance issues, which will serve as a basis for further discussion in each crop group section.

Phenylamides (PA)

The PA fungicide class, which includes mefenoxam (= metalaxyl), has well known resistance and cross resistance in various Oomycetes, though mechanism is unknown. This class, listed under FRAC Code 4, has high risk of resistance and has known resistant pathogens.[6]

Quinone outside Inhibitors (QoI)

QoI fungicides, also known as strobilurins, are "synthetic analogues of a naturally occurring compound produced by a wood rotting fungus." QoIs (FRAC Code 11) share a common anti-fungal mode of action, inhibiting respiration in cells by targeting the cytochrome bc-1 protein that is encoded by a gene in the mitochondria. Comprised of many fungicides, including four alternatives to Cyazofamid (azoxystrobin, famoxadone, fenamidone, pyraclostrobin), QoIs are broad spectrum with activity against major fungal pathogens.[7] Many have developed a high level of resistance, caused by single mutation (G143A) in the cytochrome bc-1 gene, and to a lesser extent by single mutation (F129L). FRAC guidelines for QoIs recommend instructions to apply the fungicides at specified intervals, to limit the number of applications, and to alternate or mix with applications of effective fungicides from other groups.[8] This group has known resistance in various fungal species and cross resistance is shown between all members of the QoI group. Resistance risk is high and FRAC has QoI Guidelines for resistance management.[9]

Toluamides

Toluamides, chemicals of the Benzamide group, which includes zoxamide and are listed under FRAC Code 22, have low to medium risk of resistance and resistance management is required. [10]

---

[6] *FRAC Code List 2013: Fungicides sorted by mode of action*, Fungicide Resistance Action Committee. Page 3. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Pages 9-11. (Reference 2)

[7] Damicone, John, and Damon Smith. *Fungicide Resistance Manual.* Oklahoma Cooperative Extension Service, Oklahoma State University, Page 7. (Reference 3)

[8] Brent, Keith J., Derek W. Hollman. *Fungicide Resistance in Crop Pathogens: How Can It Be Managed?* Fungicide Resistance Action Committee, 2007, Page 55. (Reference 4)

[9] *FRAC Code List 2013 Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)

[10] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 3. (Reference 1)

Cyanoacetamideoxime

Cyanoacetamideoxime fungicides, which include cymoxanil, listed under FRAC Code 27, have low to medium risk of resistance and have known resistant pathogens. Resistance management is required[11]

Carbamates

Carbamate fungicides, which include propamocarb, are listed under FRAC Code 28 and have low to medium risk resistance and have known resistant pathogens. Resistance management is required[12]

Phosphonates

Phosphonates group (FRAC Code 33), which includes fosetyl-Al and Phosphorous acid/salts, has few resistance cases reported in few pathogens. This group has low resistance risk but has known resistant pathogens.[13]

Carboxylic Acid Amides (CAA)

CAA fungicides are listed under FRAC Code 40 and include dimethomorph and mandipropamid. This group has known resistance in *Plasmopara viticola* but not in *Phytophthora infestans* and has low to medium risk of resistance. There are known pathogens for resistance to this group. Cross resistance exists between all members of the CAA group. FRAC has resistance management guidelines for CAA fungicides.[14]

Benzamides

Benzamides fungicides (FRAC Code 43), which include fluopicolide, have no known resistance or resistant pathogens to date.[15]

Multi-site contact activity

Some alternatives have multi-site contact modes of actions. Multi-site fungicides interfere with many metabolic processes of the fungus and are usually protectant fungicides. "Once taken up by fungal cells, multisite inhibitors act on processes such as general enzyme activity that disrupt numerous cell functions. Numerous mutations affecting many sites in the fungus would be necessary for resistance to develop. Typically, these fungicides inhibit spore germination and must be applied before infection occurs. Multi-site fungicides form a chemical barrier between the plant and fungus. The risk of resistance to these fungicides is

[11] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 9. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Page 41. (Reference 2)
[12] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 6. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Page 34. (Reference 2)
[13] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 9. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Page 41. (Reference 2)
[14] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 8. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Page 39. (Reference 2)
[15] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 3. (Reference 1) FRAC list of plant pathogenic organisms resistant to disease control agents, January 2013, Page 20. (Reference 2)

low."[16] Alternative multi-site fungicides include inorganics (various copper salts like copper hydroxide, copper oxychloride, copper sulfate and cuprous oxide, FRAC Code M1), dithiocarbamates (mancozeb and maneb, FRAC Code M3), phthalimides (folpet, FRAC Code M4), and chlorothalonil (FRAC Code M5). Generally considered as a low resistance risk group, no signs of resistance to these fungicides have been noted, and there is no known cross resistance between group members.[17]

3. Method Used To Identify Available Resistance Management, Pest Management, and Efficacy Information

In order to determine that Cyazofamid satisfies the statutory criteria for the extension of the exclusive use period, ISKBC followed a rigorous research and analysis methodology. The process described below was used to find resistance management, integrated pest management, and efficacy information for each of the labeled use sites. The findings from this process are detailed in sections 4 through 11. The various resources provide a significant amount of information to support that Cyazofamid meets the eligibility criteria for many minor crops.

After having confirmed the acreage and the major/minor crop status in the 2007 Census of Agriculture and OPPTS 860.1500, the pathogens and alternative fungicides were evaluated for each individual crop within the group.[18] The primary analysis consisted of reviewing three major documents from the Fungicide Resistance Action Committee: the *FRAC Pathogen Risk List December 2005*, the *FRAC List of Plant Pathogenic Organisms Resistant to Disease Control Agents Revised January 2013*, and the *FRAC Code List 2013: Fungicides sorted by mode of action (including FRAC Code numbering).* The purpose of FRAC is to "provide fungicide resistance management guidelines to prolong the effectiveness of 'at risk' fungicides and to limit crop losses should resistance occur."[19] The documents provide general information about the risk levels for certain fungal diseases of developing resistance to individual or certain classes of fungicides. The relevant information on modes of action and resistance levels for the respective pathogens and the previously determined alternative active ingredients were extracted and included in this petition.

[16] Damicone, John, and Damon Smith. *Fungicide Resistance Manual.* Oklahoma Cooperative Extension Service, Oklahoma State University. Page 3. (Reference 3)
[17] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 10. (Reference 1)
[18] United States, Environmental Protection Agency. Prevention, Pesticides and Toxic Substances. *Residue Chemistry Test Guidelines OCSPP 860.1500 Crop Field Trials.* Pages 60-62. EPA, August 1996.
[19] "About FRAC." *FRAC*. Fungicide Resistance Action Committee. http://www.frac.info/frac/index.htm (Reference 5)

4. CROP GROUP 5: BRASSICA (COLE) LEAFY VEGETABLES

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST CLUBROOT AND DOWNY MILDEW ON BRASSICA AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO DOWNY MILDEW AND CLUBROOT ON BRASSICA

Cyazofamid was registered for use against clubroot *(Plasmodiophora brassicae*) and downy mildew (*Peronospora parasitica*) on 18 minor crops (Table 4A) in Crop Group 5 (Brassica (Cole) Leafy Vegetables) on August 13, 2010.[20] United States Production statistics from USDA NASS for each of these crops are listed in Appendix 3. The crops for which there is no information in the NASS database or OPPTS 860.1500 are assumed to be below the 300,000 acre threshold and thus considered minor crops. The statistics illustrate that the use sites qualify as minor use crops under the FIFRA Sec. 2 (ll). Cyazofamid was registered on Brassica within the first seven years after the initial registration, and is eligible for extended exclusive use. ISK has evaluated the literature available on Brassica and alternative pesticides, and believes that there are insufficient efficacious alternatives available, thus meeting the exclusive use FIFRA Sec. 3(c)(1)(F)(ii) Criterion I (Insufficient Efficacious Alternatives) for Cyazofamid. In addition, ISK believes that exclusive use FIFRA Sec. 3(c)(1)(F)(ii) Criteria III (Resistance Management) and IV (Integrated Pest Management) are met for Cyazofamid as well. All criteria are discussed further below.

Clubroot is a disease that affects most plants in the cruciferous vegetable family (*Brassicaceae*) including the 18 minor crops registered for Cyazofamid. The disease is caused by the fungus *Plasmodiophora brassicae* producing a resting spore, as well as a motile spore that can swim in wet soils.[21] It can spread by any means that moves soil: wind and water, footwear and equipment, and in infected transplants. Soils that are cool, wet (70 to 80% water-holding capacity) and acidic favor the pathogen.[22]

> "It infects susceptible host plants through root hairs. Once in the tissue, it stimulates abnormal growth of affected parts, resulting in a swollen club. Infection is favored by excess soil moisture and low pH, although it can occur over a wide range of conditions. Once a plant is infected, numerous resistant spores of the fungus are produced in the "clubbed" tissues. As these tissues decay, spores are released into the soil where they can remain infectious for at least 10 years. Contaminated soil moved by wind or water can serve as a source of infestation of nearby fields, causing outbreaks of disease in areas where susceptible crops are planted for the first time. Numerous races of the pathogen have been identified."[23]

---

[20] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.

[21] Du Toit, Lindsey. *Plant Disease: Club Root of Cabbage and Other Crucifers.* Washington State University Extension. 2004. Page 2. (Reference 6)

[22] "Mustard Greens (*Brassica juncea*)-Clubroot." An Online Guide to Plant Disease Control, Oregon State University. Oregon State University Extension Service, Oregon State University. http://pnwhandbooks.org/plantdisease/mustard-greens-brassica-juncea-clubroot (Reference 7)

[23] "Diseases of Crucifers: Clubroot." *University of Rhode Island Landscape Horticulture Program, GreenShare Factsheets*. University of Rhode Island Cooperative Extension. http://www.uri.edu/ce/factsheets/prints/clubrootcrucifer.html (Reference 8)

Fluazinam is the only alternative fungicide currently labeled for use on clubroot in Brassica. Fluazinam is a contact, broad-spectrum fungicide, with a unique, multi-site mode of action that is used to control clubroot on brassica (cole) leafy vegetables, and listed under 2,6-dinitroanilines FRAC Code 29. Fluazinam has low risk of resistance, but there is resistance claimed in *Botrytis* in Japan.[24] Cyazofamid is registered and labeled for use against clubroot in 18 Brassica minor crops. Other than fluazinam, Cyazofamid is the only fungicide registered for use against clubroot in brassica (cole) vegetables, and therefore satisfies FIFRA exclusive use Criteria I, i.e. "there are insufficient efficacious alternative registered pesticides available for use".

In regard to FIFRA Sec. 3(c)(1)(F)(ii) Criterion III (Resistance Management),Table 4B below shows that there is only one other product on the market at this time for the control of clubroot on Brassica. Therefore, Cyazofamid plays a significant role in managing resistance and therefore Criterion III (in addition to Criterion I – discussed above) is met for Cyazofamid.

Downy mildew occurs wherever brassica crops are grown and infects cabbage, Brussels sprouts, cauliflower, broccoli, kale, kohlrabi, Chinese cabbage, turnip, radish, and mustard as well as cruciferous weed species. The disease caused by *Peronospora parasitica* is particularly important on seedlings but can also cause poor growth and reduced yield and quality of produce at later plant stages.[25]

Further, as stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of downy mildew of brassica leafy vegetables. RANMAN 400SC, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

Due to unique mode of action, Cyazofamid is an integral part of disease resistance management through rotation of fungicide with different mode of action.

BRASSICA (COLE) LEAFY VEGETABLES CONCLUSION:

Based on the information presented above, ISKBC believes that Cyazofamid meets FIFRA Sec. 3(c)(1)(F)(ii) Criteria I ("there are insufficient efficacious alternative registered pesticides available for the use"), III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") for all 18 crops in Crop Group 5 (Brassica (Cole) Leafy Vegetables) as listed below in Table 4A. Cyazofamid meets these criteria because it has a

[24] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)
[25] UMass Extension Vegetable Program. https://extension.umass.edu/vegetable/diseases/brassica-downy-mildew (Reference 9)

different mode of action, a moderate level of risk of developing resistance in the target pathogens, and is highly efficacious, particularly when compared to the alternative registered and marketed fungicides.

TABLE 4A: CYAZOFAMID CROP GROUP 5 (BRASSICA (COLE) LEAFY VEGETABLES) MINOR CROP QUALIFICATION – 18 CROPS QUALIFIED

Commodity	Under 300,000 Acres*
Broccoli	Yes
Broccoli, Chinese (gai lon)	Yes
Broccoli, raab (rapini)	Yes
Brussels sprouts	Yes
Cabbage	Yes
Chinese cabbage, (bok choy)	Yes
Chinese cabbage, (napa)	Yes
Chinese mustard cabbage (gai choy)	Yes
Cauliflower	Yes
Cavalo broccolo	Yes
Collards	Yes
Kale	Yes
Kohlrabi	Yes
Mizuna	Yes
Mustard greens	Yes
Mustard spinach	Yes
Rape greens	Yes
Turnip greens	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 4B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS FOR CLUBROOT AND DOWNY MILDEW TREATMENT

Pathogen	Alternative Active Ingredients	Competitor FRAC Category	Alternative Resistance Risk*	Will Cyazofamid manage resistance to this fungicide?**
Clubroot (*Plasmodiophora brassicae*)	Fluazinam	29	Low	Yes
Downy mildew (*Peronospora parasitica*)	Mefenoxam	4	High	Yes
	Fenamidone	11	High	Yes
	Phosphoric Acid	33	Low	Yes
	Dimethomorph	40	Low – Medium	Yes
	Mandipropamid	40	Low – Medium	Yes
	Maneb	M3	Low	No
	Chlorothalonil	M5	Low	No

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

5. CROP GROUP 8 (FRUITING VEGETABLES) AND OKRA

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST LATE BLIGHT AND PHYTOPHTHORA ON FRUITING VEGETABLES AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO LATE BLIGHT AND PHYTOPHTHORA BLIGHT ON FRUITING VEGETABLES

Cyazofamid was registered for use against late blight (*Phytophthora infestans*) and Phytophthora blight (*Phytophthora capsici*) on a total of 11 minor use crops (Table 5A) in Crop Group 8 and Okra on July 29, 2009.[26] Cyazofamid was registered on the crops within the first seven years after the initial registration, and therefore is eligible for extended exclusive use. United States Production statistics from USDA NASS for each of these crops are listed in Appendix 3. The crops for which there is no information in the NASS database or OPPTS 860.1500 are assumed to be below the 300,000 acre threshold and thus considered minor crops. The statistics illustrate that most of the use sites qualify as minor use crops under the statutory definition in FIFRA Sec. 2 (ll). Production of Tomato was 442,425 acres in 2007, thus this crop does not qualify for minor use criteria, as it exceeds the maximum production limit, but information on the pesticide and resistance management practices, and pathogen impacts for these crops were researched as parallel and representative of the other 11 crops, which are eligible for exclusive use

[26] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.

consideration. ISK has evaluated the literature available on alternative pesticides, the representative crops, and the entire crop group, and believes that Cyazofamid meets the exclusive use criteria III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

Cyazofamid is a unique, locally systemic fungicide from a new class of chemistry, the cyanoimidazoles, having no known resistance risk, though the resistance risk is assumed to be medium to high.[27] As discussed above in Section 1, the label for the end-use product RANMAN 400SC includes resistance management language in the directions for use section. Cyazofamid can be included in a resistance management rotation with the alternative active ingredients registered for use on fruiting-vegetables. Table 5B lists the alternative active ingredients with the corresponding level of resistance risk established by FRAC, and if Cyazofamid serves as a resistance management tool. Below, a discussion by pathogen illustrates the important role Cyazofamid plays to manage both *Phytophthora infestans* and *Phytophthora capsici* in this crop group.

Phytophthora infestans

Late blight is caused by the fungus-like Oomycete pathogen, *Phytophthora infestans*. It can infect and destroy the leaves, stems, and fruit. Severe late blight epidemics occur when the pathogen grows and reproduces rapidly host crops. Late blight has the potential to cause total crop loss.

Aside from Cyazofamid, the currently approved and labeled fungicides in these crop groups include fenamidone (FRAC Category 11) and famoxadone+cymoxanil (FRAC 11/27) mixture product which has high resistance risk due to high resistance of famoxadone[28]. Although cymoxanil only presents low to medium resistance risk, it is used as mixture with famoxadone for this fungus so that the resistance risk to the mixture is high. Other alternatives are Benzamides fungicides (FRAC 43), which include fluopicolide, and various copper salts like copper hydroxide, copper oxychloride, copper sulfate and cuprous oxide (FRAC M1). As was discussed in the alternative fungicide profiles, Benzamides fungicides have no known resistance or resistant pathogens. In order to limit the potential for developing resistance to Benzamides fungicides, rotation of fungicides is generally recommended. Cyazofamid is the only fungicide with moderate resistance risk, other than various copper salts, registered for Late blight control in fruiting vegetables. Therefore, Cyazofamid will act as a significant tool in managing the resistance of *Phytophthora infestans* in the crops listed within each crop group.

[27] *FRAC Code List 2013: Fungicides sorted by mode of action.* Fungicide Resistance Action Committee, Page 4. (Reference 1)
[28] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)

Phytophthora capsici

Phytophthora capsici is an Oomycete plant pathogen that causes Phytophthora blight and fruit rot of peppers and other important commercial crops. It is highly destructive disease that can become a serious problem during the period of heavy rainfall; the pathogen can spread rapidly through the crop resulting in severe losses within a short time. The pathogen can infect the roots, crown, stem and fruit. The alternatives to Cyazofamid used on Crop Group 8 (Fruiting vegetables) and Okra, include fenamidone, a QoI fungicide. Classified as FRAC group 11, Qol fungicides are known to be high risk for resistance and fungicide cross resistance. [29] In addition to fenamidone, the alternative fungicides include famoxadone+cymoxanil (FRAC11/27), mandipropamid (FRAC 40), fluopicolide (FRAC 43), copper (FRAC M1) and maneb (FRAC M3).

Further, as stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. RANMAN 400SC, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

CROP GROUP 8 AND OKRA CONCLUSION:

Considering the information about the pathogens, the alternative fungicides and the available crop information, ISKBC believes that Criteria III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met for all of the 10 crops in Table 5A below with less than 300,000 planted acres. Cyazofamid meets this criterion because it has a different mode of action, a moderate level of risk of developing resistance in the target pathogens, and is highly efficacious, particularly when analyzed in comparison to the alternative registered and marketed fungicides.

[29] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)

TABLE 5A: CYAZOFAMID CROP GROUP 8 (FRUITING VEGETABLES) AND OKRA MINOR CROP QUALIFICATION – 11 CROPS QUALIFIED

Commodity	Under 300,000 Acres*
Tomato	No
Eggplant	Yes
Ground cherry	Yes
Okra	Yes
Pepino	Yes
Bell pepper	Yes
Chili pepper	Yes
Cooking pepper	Yes
Pimento	Yes
Sweet pepper	Yes
Tomatillo	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 5B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Active Ingredients	FRAC Category	Alternative Resistance Risk *	Will Cyazofamid manage resistance to this fungicide?**
Late blight (Phytophthora infestans)	Fenamidone	11	High	Yes
	Famoxadone+Cymoxanil	11/27	High/Low-Med	Yes
	Fluopicolide	43	Resistance not known	Yes
	Cuprous Oxide	M1	Low	No
	Copper Hydroxide	M1	Low	No
	Copper Oxychloride	M1	Low	No
	Copper Sulfate	M1	Low	No
Phytophthora Blight (Phytophthora capsici)	Fenamidone	11	High	Yes
	Famoxadone+Cymoxanil	11/27	High/ Low – Medium	Yes
	Mandipropamid	40	Low – Medium	Yes
	Fluopicolide	43	Resistance not known	Yes
	Copper	M1	Low	No
	Maneb	M3	Low	No

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

6. CROP GROUP 9: CUCURBIT VEGETABLES

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST DOWNY MILDEW AND PHYTOPHTHORA BLIGHT ON CUCURBIT VEGETABLES AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO DOWNY MILDEW AND PHYTOPHTHORA BLIGHT ON CUCURBIT VEGETABLES

Cyazofamid was registered for use against downy mildew (*Pseudoperonospora cubensis*) and Phytophthora blight (*Phytophthora capsici*) on total of 12 minor crops in Crop Group 9 on November 12, 2004 and additional 2 minor crops (citron melon and Gherkin) in Crop Group 9 (Table 6A) on August 1, 2008.[30] United States Production statistics from USDA NASS for each of these crops are listed in Appendix 3. The crops for which there is no information in the NASS database or OPPTS 860.1500 are assumed below the 300,000 acre threshold and thus considered minor crops. The statistics from the USDA NASS database illustrate that the use sites qualify as minor use crops under the statutory definition in FIFRA Sec. 2 (ll). Cyazofamid was registered on the crops within the first seven years after the initial registration, and therefore is eligible for an extended exclusive use period. ISK has evaluated the literature available on alternative pesticides, the representative crops, and the entire crop group, and believes that Cyazofamid meets the exclusive use criteria III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

Cyazofamid is a unique, locally systemic fungicide from a new class of chemistry, the cyanoimidazoles, having no known resistance risk, though the resistance risk is assumed to be medium to high.[31] As discussed above in Section 1 above, the label for the end-use product RANMAN 400SC includes resistance management language in the directions for use section. Cyazofamid can be included in a resistance management rotation with the alternative active ingredients registered for use on Crop Group 9, Cucurbit Vegetable, most of which have high risks of developing resistance other than various copper salts. Table 6B lists the alternative active ingredients with the corresponding level of resistance risk established by FRAC, and whether Cyazofamid serves as a resistance management tool. Below, a discussion by pathogen illustrates the important role Cyazofamid plays to manage both *Phytophthora capsici* and *Pseudoperonospora cubensis* in this crop group.

[30] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.
[31] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)

Phytophthora capsici

Phytophthora blight of cucurbits is caused by the Oomycete *Phytophthora capsici*, which infects more than 50 plant species in more than 15 families, and has become one of the most serious threats to production of cucurbits and peppers as these are the most susceptible hosts[32]. It is a fast spreading, aggressive disease, capable of causing complete crop failures. The disease has been increasing in severity in the United States in recent years, where outbreaks have threatened the survival of the processing pumpkin industry[33].

The alternatives to Cyazofamid for *Phytophthora capsici* control are mefenoxam (FRAC Category 4) and famoxadone+cymoxanil (FRAC 11/27), both of which have high risk of resistance and cross resistance[34]. Further, dimethomorph and mandipropamid (FRAC 40) are also alternatives, which have low to medium resistance risk. Although phosphorous acid (FRAC 33) and fluopicolide (FRAC 43) are also alternatives with low risk or resistance risk not known, it is essential that fungicides with different modes of action be rotated to prevent the buildup of fungicide resistance in *Phytophthora capsici.*[35] As Cyazofamid has a unique mode of action, it can play a significant role in resistance management in Cucurbit vegetable crop group.

Pseudoperonospora cubensis

Downy mildew caused by *Pseudoperonospora cubensis* is one of the most important foliar diseases of cucurbits. It occurs worldwide where conditions of temperature and humidity allow its establishment and can result in major losses to cucumber, melon, squash, pumpkin, watermelon, and other cucurbits. *Pseudoperonospora cubensis* infects only members of the cucurbit family and is an obligate parasite. Its survival depends on the presence of cucurbit hosts, either in climates which permit their growth year round or in greenhouse culture.[36] Since 2004, the resurgence in virulence has caused growers great concern and substantial economic losses necessitating increased use of fungicides.

The alternatives to Cyazofamid to control *Pseudoperonospora cubensis* include famoxadone (FRAC Category 11) and famoxadone+cymoxanil. FRAC has classified group 11 fungicides as a class known to be high risk for resistance development and cross resistance occurs between all members of group 11 fungicides.[37] Further, resistance of Pseudoperonospora cubensis to

[32] APSnet, Phytophthora Blight: A Serious Threat to Cucurbit Industries. http://www.apsnet.org/publications/apsnetfeatures/Pages/PhytophthoraBlight.aspx (Reference 10)
[33] British Columbia, Agriculture, Pest Management. http://www.agf.gov.bc.ca/cropprot/pcapsici.htm (Reference 11)
[34] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Pages 3, 4 & 9. (Reference 1)
[35] Vegetable Diseases Caused by *Phytophthora capsici* in Florida, Plant Pathology Fact Sheet SP-159 (Reference 12)
[36] UmassAmherst, Center for Agriculture, UMassExtension. http://extension.umass.edu/vegetable/diseases/winter-squash-downy-mildew (Reference 13)
[37] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 4. (Reference 1)

FRAC 11 fungicides has been identified[38] and is of such magnitude that this class of fungicides is no longer recommended. In addition to the QoI compounds, other fungicides used for treatments of cucurbit vegetables include zoxamide (FRAC 22), cymoxanil (FRAC 27), propamocarb HCl (FRAC 28), and dimethomorph (FRAC 40), all of these have low to medium resistance risk. Fosetyl-Al and phosphorous acid (FRAC 33), fluopicolide (FRAC 43), various copper salts (FRAC M1), mancozeb and maneb (FRAC M3) and chlorothalonil (FRAC M5) are also alternatives and have low or no known resistance risk. With its unique mode of action, Cyazofamid serves as an effective alternative in resistance management strategies.

In addition to playing a significant role in resistance management, Cyazofamid will also play a significant role in Integrated Pest Management programs. As stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. RANMAN, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

CROP GROUP 9 CONCLUSION:

Based on the discussion above, Cyazofamid meets the Criterion III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and Criterion IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") for the 14 crops listed in Table 6A below. Cyazofamid meets these criteria because it has a unique mode of action, a low to medium level of risk of developing resistance in the target pathogens.

TABLE 6A: CYAZOFAMID CROP GROUP 9 CUCURBIT VEGETABLES MINOR CROP QUALIFICATION – 14 CROPS QUALIFIED

Commodity	Under 300,000 Acres*
Cantaloupe	Yes
Chayote	Yes
Chinese waxgourd (Chinese preserving melon)	Yes
Citron melon	Yes
Cucumber	Yes
Gherkin	Yes
Gourd	Yes
Honeydew melon	Yes
Momordica spp.	Yes
Muskmelon	Yes
Watermelon	Yes
Pumpkin	Yes
Squash	Yes
Zucchini	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

[38] *FRAC List of plant pathogenic organisms resistant to disease control agents,* January 2013, Page 25. (Reference 2)

TABLE 6B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Active Ingredients	FRAC Category	Alternative Resistance Risk *	Will Cyazofamid manage resistance to this fungicide?**
Downy mildew (*Pseudoperonospora cubensis*)	Fenamidone	11	High	Yes
	Famoxadone+Cymoxanil	11/27	High/Low-Medium	Yes
	Zoxamide	22	Low-Medium	Yes
	Cymoxanil	27	Low-Medium	Yes
	Propamocarb HCl	28	Low-Medium	Yes
	Fosetyl-Al	33	Low	Yes
	Phosphorous Acid	33	Low	Yes
	Dimethomorph	40	Low-Medium	Yes
	Fluopicolide	43	Resistance not known	Yes
	Copper	M1	Low	No
	Copper Hydroxide	M1	Low	No
	Copper Oxide	M1	Low	No
	Copper Oxychlorides	M1	Low	No
	Copper Sulfate	M1	Low	No
	Maneb	M3	Low	No
	Chlorothalonil	M3	Low	No
Phytophthora Blight (Phytophthora capsici)	Mefenoxam	4	High	Yes
	Famoxadone	11	High	Yes
	Cymoxanil	27	Low-Medium	Yes
	Phosphorous Acid	33	Low	Yes
	Dimethomorph	40	Low-Medium	Yes
	Mandipropamid	40	Low-Medium	Yes
	Fluopicolide	43	Resistance not known	Yes

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

7. CARROT

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST CAVITY SPOT, ROOT DIEBACK AND FORKING ON CARROT AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO CAVITY SPOT, ROOT DIEBACK AND FORKING ON CARROT

Cyazofamid was registered for use against 3 fungal diseases (cavity spot, root dieback, and forking) on Carrot on August 1, 2008.[39] United States Carrot Production from USDA NASS was 90,292 acres in 2007, qualifying it as minor crop under FIFRA Sec. 2 (ll) (Table 7A). Cyazofamid was registered on carrot within the first seven years after the initial registration, and is eligible for extended exclusive use. ISK has evaluated the literature available on carrot and alternative pesticides, and believes that Cyazofamid meets the exclusive use criteria I (Insufficient Efficacious Alternatives), III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

Carrot diseases caused by *Pythium* spp. are intractable problems for both growers and scientists. Carrots may be rejected at grading with only one or two visible lesions or any forking and if disease incidence exceeds a relatively low threshold it becomes uneconomical to harvest the crop.

Cyazofamid is registered for use in control of Cavity Spot (*Pythium ultimum*), Root Dieback (*P. violae, P. sulcatum*) and Forking (*P. irregulare, P. splendens*) in carrot. As shown in Table 7B, there are only 2 alternatives available for control of these diseases in carrot. Mefenoxam (FRAC Category 4) is the only other fungicide labeled for all these pathogens in carrot. Other than mefenoxam, fenamidone (FRAC 11) is labeled for Cavity Spot control in carrot. Both FRAC Categories 4 and 11 have high risk of resistance and cross resistance[40]. Cyazofamid is registered and labeled for use against Cavity Spot, Root Dieback and Forking in carrot and it is highly efficacious. Therefore, Cyazofamid satisfies FIFRA exclusive use criteria I.

As discussed above in Section 1, the label for the end-use product RANMAN 400SC includes resistance management language, and Cyazofamid can be included in a resistance management rotation with the other products labeled for use on carrot. Table 7B lists the alternatives with the corresponding level of resistance risk established by FRAC, and whether Cyazofamid serves as a resistance management tool. All the alternatives have high risk of resistance. Cyazofamid serves as an effective alternative to these compounds in resistance management strategies.

CARROT CONCLUSION:

In addition to the information from FRAC, data have been provided for carrot to demonstrate that Criterion I ("there are insufficient efficacious alternatives"), Criterion III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and Criterion IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met. Cyazofamid meets these criteria because it has a different mode of

[39] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.
[40] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Pages 3-4. (Reference 1)

action and is highly efficacious, particularly when compared to the alternative registered and marketed fungicides.

TABLE 7A: CYAZOFAMID CARROT, MINOR CROP QUALIFICATION

Commodity	Acres Below 300,000*
Carrot	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 7B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Active Ingredients	FRAC Category	Alternative Resistance Risk *	Will Cyazofamid manage resistance to this fungicide?**
Cavity Spot (Pythium ultimum)	Mefenoxam	4	High	Yes
	Fenamidone	11	High	Yes
Root Dieback (P. violae, P. sulcatum)	Mefenoxam	4	High	Yes
Forking (P. Irregulate, P. splendens)	Mefenoxam	4	High	Yes

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

8. GRAPE – EAST OF THE ROCKY MOUNTAINS

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST DOWNY MILDEW ON GRAPE EAST OF THE ROCKY MOUNTAIN AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO DOWNY MILDEW ON GRAPE EAST OF THE ROCKY MOUNTAIN

Cyazofamid was registered for use against downy mildew (Plasmopara viticola) on grapes (East of the Rocky Mountain) on July 29, 2009.[41] United States total grape production from USDA NASS was 1,051,407 acres in 2007 but excluding California State (868,330 acres), Washington State (61,056 acres) and Oregon State (18,192 acres), grape production area in East of the Rocky Mountains is 102,829 acres; hence qualifying it as minor crop under FIFRA Sec. 2 (ll) (see Table 8A). Cyazofamid was registered on the crop within the first seven years after the initial

[41] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.

registration, and is eligible for extended exclusive use. ISKBC has evaluated the literature available on grapes and alternative pesticides, and believes that Cyazofamid meets the exclusive use criteria III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

Downy mildew is a widespread, serious disease of grapevines.[42] Downy mildew is caused by the fungus *Plasmopara viticola*, which overwinters as dormant spores within infected leaves on the vineyard floor which become active in the spring. The fungus *Plasmopara viticola* can infect berries, leaves and young shoots. It occurs wherever it is wet and warm during the growing season. Fungicides, however, are the most important control measure, especially on susceptible varieties.[43]

Alternatives listed in Table 8B include fenamidone (FRAC 11), which has high risk of resistance development, and famoxadone+cymoxanil (FRAC 11/27), which also have high resistance risk as a mixture, and mandipropamid (FRAC 40), which has low to medium risk of resistance. *Plasmopara viticola* in vines has known resistance to Cyanoacetamideoximes, which include cymoxanil and CAA fungicides, which includes mandipropamid[44]. Further, fluopicolide (FRAC 43) is also an alternative with resistance risk not known. Besides these and various copper salts (RFAC M1), phosphorous acid (FRAC 33), mancozeb and ziram (FRAC M3) have low risk of resistance. Although there are some low resistance risk alternatives or an alternative with no known resistance risk, rotational use of different mode of action fungicide is an important practice in resistance management. Cyazofamid can serve as an effective alternative to these compounds in resistance management strategies.

As discussed above in Section 1, the label for the end-use product RANMAN 400SC includes resistance management language, and Cyazofamid can be included in a resistance management rotation with the other products labeled for use on grapes. Table 8B lists the alternatives with the corresponding level of resistance risk established by FRAC, and whether Cyazofamid serves as a resistance management tool. All the alternatives have high risk of resistance. Cyazofamid can serve as an effective alternative to these compounds in resistance management strategies.

GRAPE – EAST OF ROCKY MOUNTAINS CONCLUSION:

Considering the information about the pathogen, the alternative fungicides and the available crop information, ISKBC believes that Criteria III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met for grapes in East of Rocky Mountains in Table 8A below with less than 300,000 planted acres. Cyazofamid meets these criteria because it has a different mode of action, a moderate level of risk of developing resistance in the target pathogen, and is highly efficacious, particularly when compared to the alternative registered and marketed fungicides.

[42] http://www.grapes.msu.edu/downy mildew.htm (Reference 14)
[43] PennState College of Agricultural Sciences. http://agsci.psu.edu/fphg/grapes/disease-descriptions-and-management/downy_mildew (Reference 15)
[44] *FRAC List of plant pathogenic organisms resistant to disease control agents.* January 2013, Pages 39 & 41. (Reference 2)

TABLE 8A: CYAZOFAMID GRAPE EAST OF THE ROCKY MOUNTAIN, MINOR CROP QUALIFICATION

Commodity	Acres Below 300,000*
Grape, East of the Rocky Mountain	102,829 = 1,051,407 (US total) – 868,330 (California) – 61,056 (Washington) – 18,192 (Oregon)

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 8B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Alternative Active Ingredients	Competitor FRAC Category	Alternative Resistance Risk*	Will Cyazofamid manage resistance to this fungicide?**
Downy mildew (*Plasmopara viticola*)	Fenamidone	11	High	Yes
	Famoxadone+Cymoxanil	11/27	High/Low-Medium	Yes
	Phosphorous Acid	33	Low	Yes
	Mandipropamid	40	Low – Medium	Yes
	Fluopicolide	43	Resistance not known	Yes
	Copper Oxychlorides	M1	Low	No
	Copper Hydroxide	M1	Low	No
	Copper Sulfate	M1	Low	No
	Mancozeb	M3	Low	No
	Ziram	M3	Low	No

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

9. TOMATO GREENHOUSE TRANSPLANT

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST PHYTHIUM DAMPING-OFF ON TOMATO GREENHOUSE TRANSPLANT AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO PHYTHIUM DAMPING-OFF ON TOMATO GREENHOUSE TRANSPLANT

Cyazofamid was registered for use against Pythium Damping Off (*Pythium* spp.) on July 29, 2009.[45] United States Tomato Greenhouse Transplant Production from USDA NASS was 1,009 acres (43,947,871 sqft) in 2007, qualifying it as minor crop under FIFRA Sec. 2 (ll) (see Table 9A). Cyazofamid was registered on tomato greenhouse transplant within the first seven years after the initial registration, and is eligible for extended exclusive use. ISK has evaluated the literature available on tomato greenhouse transplant and alternative pesticides, and believes that Cyazofamid meets the exclusive use Criteria I (Insufficient Efficacious Alternatives), III (Resistance Management), and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

Damping Off *(Pythium* spp.*)*

Pythium species are fungal-like organisms (Oomycetes), commonly referred to as water molds, which naturally exist in soil and water as saprophytes, feeding on organic matter. Some *Pythium* species can cause serious diseases on greenhouse vegetable crops resulting in significant crop losses. *Pythium* infection leads to damping off in seedlings and crown and root rot of mature plants. In Canada, several *Pythium* species, including *P. aphanidermatum, P. irregulare* and *P. ultimum*, are known to cause damping-off and crown and root rot in greenhouse cucumber, pepper and tomato crops. There are no *Pythium* resistant varieties available although some varieties may have disease tolerance. Over watering, poor root aeration, root injury and improper root zone temperatures can weaken the crop and, thus, trigger *Pythium* outbreaks. Saturated growing media that are either too cold or too warm can be conducive to *Pythium* build up and spread in water and recirculating nutrient solution. Plants grown under optimal environmental conditions are less susceptible to *Pythium* than plants grown under poor conditions.[46]

There are no marketing data available specifically for greenhouse tomatoes. ISKBC has done a vigorous search for fungicides used for damping off on greenhouse tomatoes and found a few alternatives as shown in Table 9B. Resistance and cross resistance are well known in various Oomycetes with acylalanines chemical group (FRAC Category 4), which includes Mefenoxam, and has high risk of resistance[47]. Propamocarb HCl (FRAC 28) has known resistance with Pythium spp., particularly in glasshouse[48] , although general resistance risk is low to medium[49]. Although fosetyl-Al has low risk of resistance, rotation of registered fungicides with different chemical groups is recommended to avoid resistance development in *Pythium* spp.[50] Cyazofamid is

[45] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.
[46] British Columbia, Ministry of Agriculture, *Pythium* Diseases of Greenhouse Vegetable Crops. www.agf.gov.bc.ca/cropprot/pythium.htm (Reference 16)
[47] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Page 3. (Reference 1)
[48] *FRAC List of plant pathogenic organisms resistant to disease control agents,* January 2013, Page 34. (Reference 2)
[49] *FRAC Code List 2013: Fungicides sorted by mode of action.* Fungicide Resistance Action Committee, Page 6. (Reference 1)
[50] British Columbia, Ministry of Agriculture, *Pythium* Diseases of Greenhouse Vegetable Crops. www.agf.gov.bc.ca/cropprot/pythium.htm (Reference 16)

efficacious against damping-off and can serve as an effective alternative to these compounds in resistance management strategies.

Further, as stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. RANMAN 400SC, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

TOMATO GREENHOUSE TRANSPLANT CONCLUSION:

Considering the information about the pathogen, the alternative fungicides and the available crop information, ISKBC believes that Criteria I (Insufficient Efficacious Alternatives), III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met for tomato greenhouse transplant in Table 9A below with less than 300,000 planted acres. Cyazofamid meets these criteria because it has a different mode of action, a moderate level of risk of developing resistance in the target pathogen, and is highly efficacious, particularly when compared to the alternative registered and marketed fungicides.

TABLE 9A: CYAZOFAMID TOMATO GREENHOUSE TRANSPLANT, MINOR CROP QUALIFICATION

Commodity	Acres Below 300,000*
Tomato Greenhouse Transplant	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 9B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Alternative Active Ingredients	Competitor FRAC Category	Alternative Resistance Risk*	Will Cyazofamid manage resistance to this fungicide?**
Pythium Damping-off (*Pythium spp.*)	Mefenoxam	4	High	Yes
	Propamocarb HCl	28	Low - Medium	Yes
	Fosetyl-Al	33	Low	Yes

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

10. SPINACH

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST WHITE RUST ON SPINACH AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO WHITE RUST ON SPINACH

Cyazofamid was registered for use against white rust (*Albugo occidentalis*) on spinach on August 13, 2010.[51] United States Spinach Production from USDA NASS was 44,071 acres in 2007, qualifying it as minor crop under FIFRA Sec. 2 (ll) (see Table 10A). Cyazofamid was registered on spinach within the first seven years after the initial registration, and is eligible for extended exclusive use. ISK has evaluated the literature available on spinach and alternative pesticides, and believes that Cyazofamid meets the exclusive use criteria III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

White rust (*Albugo occidentalis*) is a major fungal disease of spinach in the United States. When it does appear it has the potential to cause economic damage by making the spinach unmarketable. Symptoms of the disease first appear as yellow spots on the upper side of the leaf similar to downy mildew. However when the leaf is flipped over to expose the underside of the leaf, a cluster of white pustules are observed instead of a mat of grey or purplish downy growth as seen in downy mildew.[52]

Alternatives to Cyazofamid with low resistance risk are very limited (Table 10B). Most of alternatives have high resistance risk. Mefenoxam (FRAC Category 4) and QoI fungicides (FRAC 11), which include azoxystrobin, fenamidone, pyraclostrobin and famoxadone, have high risk of resistance and cross resistance within each group.[53] Although famoxadone is sold and used as a mixture with cymoxanil, which has low risk of resistance, due to the high resistance risk of famoxadone, this mixture would have high resistance risk. Fosetyl-Al and copper hydroxide are low risk alternatives.

Further, as stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. RANMAN, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

[51] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.
[52] Ontario Ministry of Agriculture, Food and Rural Affairs. http://onvegetables.com/2011/05/09/white-rust-in-spinach/ (Reference 17)
[53] *FRAC Code List 2013: Fungicides sorted by mode of action*. Fungicide Resistance Action Committee, Pages 3-4. (Reference 1)

SPINACH CONCLUSION:

Considering the information about the pathogen, the alternative fungicides and the available crop information, ISKBC believes that Criteria III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met for spinach in Table 10A below with less than 300,000 planted acres. Cyazofamid meets these criteria because it has a different mode of action, a moderate level of risk of developing resistance in the target pathogen, and is highly efficacious, particularly when compared to the alternative registered and marketed fungicides.

TABLE 10A: CYAZOFAMID SPINACH, MINOR CROP QUALIFICATION

Commodity	Acres Below 300,000*
Spinach	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 10B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Alternative Active Ingredients	Competitor FRAC Category	Alternative Resistance Risk*	Will Cyazofamid manage resistance to this fungicide?**
White Rust (*Albugo occidentalis*)	Mefenoxam	4	High	Yes
	Azoxystrobin	11	High	Yes
	Fenamidone	11	High	Yes
	Pyraclostrobin	11	High	Yes
	Famoxadone/Cymoxanil	11/27	High/Low-Medium	Yes
	Fosetyl-Al	33	Low	Yes
	Copper Hydroxide	M1	Low	No

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

11. HOP

CYAZOFAMID IS A HIGHLY EFFICACIOUS REGISTERED PESTICIDE AGAINST DOWNY MILDEW ON HOP AND CYAZOFAMID PLAYS OR WILL PLAY A SIGNIFICANT PART IN INTEGRATED PEST MANAGEMENT AND MANAGING PEST RESISTANCE TO DOWNY MILDEW ON HOP

Cyazofamid was registered for use against downy mildew (*Pseudoperonospora humuli*) on hop on August 13, 2008.[54] United States Hop Production from USDA NASS was 31,145 acres in 2007, qualifying it as minor crop under FIFRA Sec. 2 (ll) (see Table 11A). Cyazofamid was registered on hop within the first seven years after the initial registration, and is eligible for extended exclusive use. ISK has evaluated the literature available on hops and alternative pesticides, and believes that Cyazofamid meets the exclusive use criteria III (Resistance Management) and IV (Integrated Pest Management) under FIFRA Sec. 3(c)(1)(F)(ii).

The hop plant (*Cumulus lupus L.*) is a perennial with clockwise twining vine that dies back to the ground each year. The male and female flowers are borne on separate plants. The papery bracts and bracteoles of mature hop corns are used almost exclusively to flavor fermented malt beverages. Hop downy mildew, caused by *Pseudoperonospora humuli* (*P. humuli*) is a major disease in many hop-growing areas.[55] *P. humuli* is closely related to the downy mildew that we can find on crops such as cucumbers and watermelons, but is not so closely related that the downy mildew from squash will infect hops and vice versa. Downy mildew can cause the complete loss of marketable hop yield, and even hill death in sensitive varieties. It is a very serious hindrance to successful hops production, but diligent integrated pest management can help reduce disease infection.[56]

Losses due to downy mildew occur at several points in the disease cycle. Crown infections can result in crown rot and plant death. Bud infections do not cause plant death, but do contribute to poor plant vigor. Vine infections reduce vine before and may spike the growing point necessitating retraining and increasing labor costs. Downy mildew thrives in environments with moderate temperature, high humidity, and frequent precipitation. Whenever possible, resistant varieties should be planted in fields known to have conditions favoring disease development. Cultural practices that increase air movement, decreases relative humidity, and increase summer temperatures will also help control downy mildew. When conditions favoring disease development prevail, cultural practices and plant resistance may fail to provide adequate control. Under these conditions, chemical fungicides are used for downy mildew control.[57]

[54] Office of Prevention, Pesticides and Toxic Substances. "RANMAN 400SC EPA Registration No. 71512-3 Amendments and Submissions Dated: August 1, 2008 (Added use for Carrot); July 29, 2009 (Added use for Grapes, East of the Rocky Mountain and Fruiting Vegetables and Okra); and August 13, 2010 (Added use for Brassica (Cole) Leafy Vegetables, Hops and Spinach.)" Environmental Protection Agency, Washington, DC.
[55] Control of Downy Mildew of Hops, Plant Disease/November 1983, Pages 1183-1185. (Reference 18)
[56] Managing Downy Mildew in Hops in the Northeast, University of Vermont Extension, June 2012 (Reference 19)
[57] University of Idaho, Department of Plant, Soil, & Entomological Sciences.
http://www.cals.uidaho.edu/pses/Research/r_ent_hoppest_downymildew.htm (Reference 20)

Alternatives include mefenoxam (FRAC Category 4) and famoxadone+cymoxanil mixture (FRAC 11/27) which have high resistance risk. Other alternatives are cymoxanil (FRAC 27); fosetyl-al and phosphorous acid (FRAC 33); dimethomorph and mandipropamid (FRAC 40); copper sulfate and oxide salts (FRAC M1); and folpet (FRAC M1), all of which have low or low to medium resistance risk. Although Cyazofamid has medium to high resistance risk, it is a good rotation fungicide to these alternatives (see Table 11B).

Further, as stated in "Profile for Cyazofamid" section, Cyazofamid has IPM language in its label and is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. RANMAN, formulated commercial product of Cyazofamid, is recommended for use as part of an IPM program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage.

HOP CONCLUSION:

Considering the information about the pathogen, the alternative fungicides and the available crop information, ISKBC believes that Criteria III ("the minor use pesticide plays or will play a significant part in managing pest resistance") and IV ("the minor use pesticide plays or will play a significant part in an integrated pest management program") have been met for hop in Table 11A below with less than 300,000 planted acres. Cyazofamid meets these criteria because it has a different mode of action, a moderate level of risk of developing resistance in the target pathogen, and is highly efficacious, particularly when analyzed in comparison to the alternative registered and marketed fungicides.

TABLE 11A: CYAZOFAMID HOP, MINOR CROP QUALIFICATION

Commodity	Acres Below 300,000*
Hop	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.

TABLE 11B: CYAZOFAMID WILL PLAY A ROLE IN MANAGING PEST RESISTANCE TO THE ALTERNATIVE ACTIVE INGREDIENTS

Pathogen	Alternative Active Ingredients	Competitor FRAC Category	Alternative Resistance Risk*	Will Cyazofamid manage resistance to this fungicide?**
Downy mildew (*Pseudoperonospora humuli*)	Mefenoxam (Metalaxyl)	4	High	Yes
	Famoxadone+Cymoxanil	11/27	High/Low-Medium	Yes
	Cymoxanil	27	Low – Medium	Yes
	Fosetyl-Al	33	Low	Yes
	Phosphorous Acid	33	Low	Yes
	Dimethomorph	40	Low - Medium	Yes
	Mandipropamid	40	Low – Medium	Yes
	Copper Sulfate/Oxide	M1	Low	No
	Folpet	M4	Low	No

* FRAC Code List 2013: Fungicides sorted by mode of action

** This was determined primarily on the basis of the FRAC codes and modes of actions for the alternatives: if the risk of resistance (based on the FRAC code) for an alternative active ingredient is classified as M (multi-site), it was concluded that Cyazofamid would not serve as a resistance management tool; if the risk of resistance (based on the FRAC code) for an alternative active ingredient was Low to Medium or High, Cyazofamid was considered to be a resistance management tool.

CONCLUSIONS

ISKBC, after rigorous review and analysis of many different data sources has confirmed that the following Cyazofamid minor crops meet the following FIFRA Sec. 3(c)(1)(F)(ii) exclusive use criteria:

CROP	NUMBER OF MINOR USES	EXCLUSIVE USE CRITERIA MET
Crop Group 5 (Brassica (cole) leafy vegetables)	18 (see Table 4A)	Criteria I, III and IV
Crop group 8 (FRUTING VEGETABLE) AND OkRA	11 (see Table 5A)	Criteria III and IV
Crop group 9 (CUCURBIT VEGETABLE)	14 (see Table 6A)	Criteria III and IV
CARROT	1	Criteria I, III and IV
GRAPE,EAST OF THE ROCKY MOUNTAINS	1	Criteria III and IV
TOMATO GREENHOUSE TRANSPLANT	1	Criteria I, III and IV
SPINACH	1	Criteria III and IV
HOP	1	Criteria III and IV

FIFRA Sec. 3(c)(1)(F)(ii) states that for each 3 minor uses registered within 7 years of the commencement of the exclusive use period that 1 additional year (up to a maximum of 3 years) of exclusive use data protection can be granted assuming that the minor uses meet one of the four exclusive use criteria. The exclusive use period for Cyazofamid commenced November 9, 2004 when Cyazofamid technical was registered and all of the above uses were granted on November 12, 2004, August 1, 2008, July 29, 2009 and August 13, 2010, which are within the 7 year requirement. Therefore, all of the uses above are eligible to be counted towards the three year extension as long as they meet at least one of the exclusive use criteria. As this document has shown (and as the table above summarizes), all of the uses meet at least one criteria, which gives a total of 48 minor uses. As only 9 uses are needed to obtain the maximum of 3 years of exclusive use data protection, ISKBC requests that three years of exclusive use data protection be granted for the following Cyazofamid registrations: 71512-2 (Cyazofamid Technical) and 71512-3 (RANMAN 400SC).

REFERENCES (ORDER of APPEARANCE)

1. *FRAC Code List 2013*: Fungicides sorted by mode of action, Fungicide Resistance Action Committee, Page 3.
2. FRAC List of Plant Pathogenic Organisms Resistant to Disease Control Agents, January 2013, Pages 9-11.
3. Damicone, John, and Damon Smith. *Fungicide Resistance Manual.* Oklahoma Cooperative Extension Service, Oklahoma State University, Page 7.
4. Brent, Keith J., Derek W. Hollman. *Fungicide Resistance in Crop Pathogens: How Can it be Managed?* Fungicide Resistance Action Committee, 2007, Page 55.
5. "About FRAC." *FRAC*. Fungicide Resistance Action Committee.
6. Du Toit, Linsey. *Plant Disease: Club Root of Cabbage and Other Crucifers.* Washington State University Extension. 2004. Page 2.
7. "Mustard Greens *(Brassica juncea)*-Clubroot." An Online Guide to Plant Disease Control, Oregon State University. Oregon State University Extension Service.
8. "Diseases of Crucifers: Clubroot." *University of Rhode Island Landscape Horticulture Program, GreenShare Factsheets.* University of Rhode Island Cooperative Extension.
9. UMass Extension Vegetable Program.
10. APSnet, Phytophthora Blight: A Serious Threat to Cucurbit Industries.
11. British Columbia, Agriculture, Pest Management.
12. Vegetable Diseases Caused by *Phytophthora capsici* in Florida, Plant Pathology Fact Sheet SP-159.
13. UmassAmherst, Center for Agriculture, UMassExtension.
14. http://www.grapes.msu.edu/downy mildew.htm
15. PennState College of Agricultural Sciences.
16. British Columbia, Ministry of Agriculture, *Pythium* Diseases of Greenhouse Vegetable Crops.
17. Ontario Ministry of Agriculture, Food and Rural Affairs.
18. Control of Downy Mildew of Hops, Plant Disease/November 1983, Pages 1183-1185.
19. Managing Downy Mildew in Hops in the Northeast, University of Vermont Extension, June 2012.
20. University of Idaho, Department of Plant, Soil, & Entomological Sciences.

Reference 1

Footnotes: 6, 9, 10, 11, 12, 13, 14, 15, 17, 24, 27, 28, 29, 31, 34, 37, 40, 47, 49, and 53

FRAC Code List ©*2013: 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. The letters refer to P = host plant defence inducers, M = multi-site inhibitors, and U = unknown mode of action and unknown resistance risk. Reclassification of compounds based on new research may result in codes to expire. This is most likely in the U – section when the mode of actions gets clarified. These codes are not re-used for new groups; a note is added to indicate reclassification into a new code.

Last update: February 2013
Next update decisions: December 2013

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
A: nucleic acids synthesis	**A1:** RNA polymerase **I**	**PA** – fungicides (**P**henyl**A**mides)	acylalanines	benalaxyl benalaxyl-M (=kiralaxyl) 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 in fungi unknown. Resistance management required.	**31**
B: mitosis and cell division	**B1:** ß-tubuline assembly in mitosis	**MBC** - fungicides (**M**ethyl **B**enzimidazole **C**arbamates)	benzimidazoles	benomyl carbendazim fuberidazole thiabendazole	Resistance common in many fungal species. Several target site mutations, mostly E198A/G/K, F200Y in β-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: ß-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: ß-tubulin assembly in mitosis	benzamides	toluamides	zoxamide	Low to medium risk. Resistance management required.	**22**
		thiazole carboxamide	ethylamino-thiazole carboxamide	ethaboxam		
	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
C. respiration	**C1:** complex I NADH Oxido-reductase	pyrimidinamines	pyrimidinamines	diflumetorim	Resistance not known.	**39**
		pyrazole-MET1	pyrazole-5-carboxamides	tolfenpyrad		
	C2: complex II: succinate-dehydro-genase	SDHI (**S**uccinate **deh**ydrogenase **i**nhibitors)	phenyl-benzamides	benodanil flutolanil mepronil	Resistance known for several fungal species in field populations and lab mutants. Target site mutations in sdh gene, e.g. H/Y (or H/L) at 257, 267, 272 or P225L, dependent on fungal species. Resistance management required. **Medium to high risk.** **See FRAC SDHI Guidelines for resistance management.**	**7**
			phenyl-oxo-ethyl thiophene amide	isofetamid		
			pyridinyl-ethyl-benzamides	fluopyram		
			furan- carboxamides	fenfuram		
			oxathiin-carboxamides	carboxin oxycarboxin		
			thiazole-carboxamides	thifluzamide		
			pyrazole-4-carboxamides	benzovindiflupyr bixafen fluxapyroxad furametpyr isopyrazam penflufen penthiopyrad sedaxane		
			pyridine-carboxamides	boscalid		
	C3: complex III: cytochrome bc1 (ubiquinol oxidase) at Qo site *(cyt b gene)*	**QoI**-fungicides (**Q**uinone **o**utside **I**nhibitors)	methoxy-acrylates	azoxystrobin coumoxystrobin enoxastrobin flufenoxystrobin picoxystrobin pyraoxystrobin	Resistance known in various fungal species. Target site mutations in cyt b gene (G143A, F129L) and additional mechanisms. Cross resistance shown between all members of the QoI group. **High risk.** **See FRAC QoI Guidelines for resistance management.**	**11**
			methoxy-carbamates	pyraclostrobin pyrametostrobin triclopyricarb		
			oximino acetates	kresoxim-methyl trifloxystrobin		
			oximino-acetamides	dimoxystrobin fenaminstrobin metominostrobin orysastrobin		
			oxazolidine-diones	famoxadone		
			dihydro-dioxazines	fluoxastrobin		
			Imidazolinones	fenamidone		
			benzyl-carbamates	pyribencarb		
	C4: complex III: cytochrome bc1(ubiquinone reductase) at Qi site	**QiI** - fungicides (**Q**uinone **i**nside **I**nhibitors)	cyano- imidazole	cyazofamid	Resistance risk unknown but assumed to be medium to high (mutations at target site known in model organisms). Resistance management required.	**21**
			sulfamoyl-triazole	amisulbrom		
	C5: uncouplers of oxidative phos-phorylation		dinitrophenyl crotonates	binapacryl meptyldinocap dinocap	Resistance not known. Also acaricidal activity.	**29**
			2,6-dinitro-anilines	fluazinam	Low risk. However, resistance claimed in *Botrytis* in Japan.	
			(pyr.-hydrazones)	(ferimzone)	Reclassified to U 14 in 2012.	

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
C: respiration (continued)	**C6:** inhibitors of oxidative phos-phorylation, ATP synthase	organo tin compounds	tri phenyl tin compounds	fentin acetate fentin chloride fentin hydroxide	Some resistance cases known. Low to medium risk.	**30**
	C7: ATP production (proposed)	thiophene-carboxamides	thiophene-carboxamides	silthiofam	Resistance reported. Risk low.	**38**
	C8: complex III: cytochrome bc1 (ubiquinone reductase) at Q x (unknown) site	QxI – fungicide (Quinone x Inhibitor)	triazolo-pyrimidylamine	ametoctradin	Resistance risk assumed to be medium to high (single site inhibitor). Resistance management required.	**45**
D: amino acids and protein synthesis	**D1:** methionine biosynthesis (proposed) *(cgs gene)*	**AP -** fungicides (**A**nilino-**P**yrimidines)	anilino-pyrimidines	cyprodinil mepanipyrim pyrimethanil	Resistance known in *Botrytis* and *Venturia*, sporadically in *Oculimacula* . **Medium risk.** **See FRAC Anilinopyrimidine Guidelines for resistance management.**	**9**
	D2: protein synthesis	enopyranuronic acid antibiotic	enopyranuronic acid antibiotic	blasticidin-S	Low to medium risk. Resistance management required.	**23**
	D3: protein synthesis	hexopyranosyl antibiotic	hexopyranosyl antibiotic	kasugamycin	Resistance known in fungal and bacterial (*P. glumae*) pathogens. Medium risk. Resistance management required.	**24**
	D4: protein synthesis	glucopyranosyl antibiotic	glucopyranosyl antibiotic	streptomycin	Bactericide. Resistance known. High risk. Resistance management required.	**25**
	D5: protein synthesis	tetracycline antibiotic	tetracycline antibiotic	oxytetracycline	Bactericide. Resistance known. High risk. Resistance management required.	**41**
E: signal transduction	**E1:** signal transduction (mechanism unknown)	aza-naphthalenes	aryloxyquinoline	quinoxyfen	Resistance to quinoxyfen known. Medium risk. Resistance management required. Cross resistance found in *Erysiphe (Uncinula) necator* but not in *Blumeria graminis*.	**13**
			quinazolinone	proquinazid		
	E2: MAP/Histidine-Kinase in osmotic signal transduction *(os-2, HOG1)*	**PP**-fungicides (**P**henyl**P**yrroles)	phenylpyrroles	fenpiclonil fludioxonil	Resistance found sporadically, mechanism speculative. Low to medium risk. Resistance management required.	**12**

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
E: signal transduction (continued)	**E3:** MAP/Histidine-Kinase in osmotic signal transduction *(os-1, Daf1)*	dicarboximides	dicarboximides	chlozolinate iprodione procymidone vinclozolin	Resistance common in *Botrytis* 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**
F: lipid synthesis and membrane integrity	**F1:**	formerly dicarboximides				
	F2: phospholipid biosynthesis, methyltrans-ferase	phosphoro-thiolates	phosphoro-thiolates	edifenphos iprobenfos (IBP) pyrazophos	Resistance known in specific fungi. Low to medium risk. Resistance management required if used for risky pathogens.	**6**
		dithiolanes	Dithiolanes	isoprothiolane		
	F3: lipid peroxidation (proposed)	**AH**-fungicides (**A**romatic **H**ydrocarbons) (chlorophenyls, nitroanilines)	aromatic hydrocarbons	biphenyl chloroneb dicloran quintozene (PCNB) tecnazene (TCNB) tolclofos-methyl	Resistance known in 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)	carbamates	Carbamates	iodocarb propamocarb prothiocarb	Low to medium risk. Resistance management required.	**28**
	F5:	**formerly CAA**-fungicides				
	F6: microbial disrupters of pathogen cell membranes	microbial (*Bacillus* sp.)	*Bacillus* sp. and the fungicidal lipopeptides produced	*Bacillus amyloliquefaciens* strain QST 713 *Bacillus amyloliquefaciens* strain FZB24 *Bacillus amyloliquefaciens* strain MBI600 *Bacillus amyloliquefaciens* strain D747	Resistance not known. Induction of host plant defence described as additional mode of action for strain FZB24	**44**
	F7: cell membrane disruption (proposed)	plant extract	terpene hydrocarbons and terpene alcohols	extract from *Melaleuca alternifolia* (tea tree)	Resistance not known	**46**

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL GROUP	COMMON NAME	COMMENTS	FRAC CODE
G: sterol biosynthesis in membranes	**G1:** C14- demethylase in sterol biosynthesis *(erg11/cyp51)*	**DMI**-fungicides (**De**-**M**ethylation **I**nhibitors) (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 (erg 11) 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. **Medium risk.** **See FRAC SBI Guidelines for resistance management.**	**3**
			pyridines	pyrifenox pyrisoxazole		
			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 simeconazole tebuconazole tetraconazole triadimefon triadimenol triticonazole		
			triazolinthiones	prothioconazole		
	G2: Δ^{14}-reductase and $\Delta^{8}\rightarrow\Delta^{7}$-isomerase in sterol biosynthesis *(erg24, erg2)*	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. **Low to medium risk.** **See FRAC SBI Guidelines for resistance management.**	**5**
			piperidines	fenpropidin piperalin		
			spiroketal-amines	spiroxamine		
	G3: 3-keto reduc-tase, C4- de-methylation *(erg27)*	(SBI: Class III)	hydroxyanilides	fenhexamid	Low to medium risk. Resistance management required.	**17**
			amino-pyrazolinone	fenpyrazamine		
	G4: squalene-epoxidase in sterol biosynthesis *(erg1)*	(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
H: cell wall biosynthesis	**H3:** trehalase and inositol-biosynthesis	glucopyranosyl antibiotic	glucopyranosyl antibiotic	validamycin	Resistance not known	**26**
	H4: chitin synthase	polyoxins	peptidyl pyrimidine nucleoside	polyoxin	Resistance known. Medium risk. Resistance management required.	**19**
	H5: cellulose synthase	**CAA**-fungicides (**C**arboxylic **A**cid **A**mides)	cinnamic acid amides	dimethomorph flumorph pyrimorph	Resistance known in *Plasmopara viticola* but not in *Phytophthora infestans*. Cross resistance between all members of the CAA group. **Low to medium risk. See FRAC CAA Guidelines for resistance management**	**40**
			valinamide carbamates	benthiavalicarb iprovalicarb valifenalate		
			mandelic acid amides	mandipropamid		
I: melanin synthesis in cell wall	**I1:** reductase in melanin biosynthesis	**MBI-R** (**M**elanin **B**iosynthesis **I**nhibitors – **R**eductase)	isobenzo-furanone	fthalide	Resistance not known	**16.1**
			pyrrolo-quinolinone	pyroquilon		
			triazolobenzo-thiazole	tricyclazole		
	I2: dehydratase in melanin biosynthesis	**MBI-D** (**M**elanin **B**iosynthesis **I**nhibitors – **D**ehydratase)	cyclopropane-carboxamide	carpropamid	Resistance known. Medium risk. Resistance management required.	**16.2**
			carboxamide	diclocymet		
			propionamide	fenoxanil		
P: host plant defence induction	**P1:** salicylic acid pathway	benzo-thiadiazole BTH	benzo-thiadiazole BTH	acibenzolar-S-methyl	Resistance not known	**P**
	P2	benzisothiazole	benzisothiazole	probenazole (also antibacterial and antifungal activity)	Resistance not known	
	P3	thiadiazole-carboxamide	thiadiazole-carboxamide	tiadinil isotianil	Resistance not known	
	P4	natural compound	polysaccharides	laminarin	Resistance not known	
	P5	plant extract	complex mixture, ethanol extract	extract from *Reynoutria sachalinensis* (giant knotweed)	Resistance not known	

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**
				phophorous 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-sulphonamides	flusulfamide	Resistance not known	**36**
	unknown	pyridazinones	pyridazinones	diclomezine	Resistance not known	**37**
	unknown	thiocarbamate	thiocarbamate	methasulfocarb	Resistance not known	**42**
	unknown	phenyl-acetamide	phenyl-acetamide	cyflufenamid	Resistance in *Sphaerotheca*. Resistance management required	**U6**
	actin disruption (proposed)	aryl-phenyl-ketone	benzophenone	metrafenone	Less sensitive isolates detected in wheat powdery mildew. Medium risk. Resistance management required.	**U8**
			benzoylpyridine	pyriofenone		
	Cell membrane disruption (proposed)	guanidines	guanidines	dodine	Resistance known in *Venturia inaequalis.* Low to medium risk. Resistance management recommended.	**U12**
	unknown	thiazolidine	cyano-methylene-thiazolidine	flutianil	Resistance not known	**U13**
	unknown	pyrimidinone-hydrazones	pyrimidinone-hydrazones	ferimzone	Resistance not known Reclassified from C5 in 2012	**U14**
not clas-si-fied	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
Multi-site contact activity	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	**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	guazatine iminoctadine		**M7**
		triazines	triazines	anilazine		**M8**
		quinones (anthraquinones)	quinones (anthra-quinones)	dithianon		**M9**
		quinoxalines	quinoxalines	chinomethionat / quinomethionate		**M10**
		maleimide	maleimide	fluoroimide		**M11**

Reference 2

Footnotes: 6, 11, 12, 13, 14, 15, 38, 44, and 48

FRAC
LIST OF PLANT PATHOGENIC ORGANISMS RESISTANT TO DISEASE CONTROL AGENTS

Revised January 2013

Source: www.frac.info
January 2013

Important notes

The scope of the list.

The FRAC codes used in this document refer to those used in the FRAC Code List. The entries are listed by their Mode of Action code, with the Chemical Group Codes and Group Names also being given for reference. *For more information please refer to the latest edition of the FRAC Code list*.

This list is extensive in identifying those plant pathogens that have shown some form of resistance to the modes of action given and to the respective chemical groups. Where a FRAC Code is not listed, no resistance has been reported.

Entries have generally been selected as the first confirmed, published, case of resistance of the particular mode of action against the pathogen listed. Subsequent references for the same mode of action and host-pathogen combination are only included if the information is considered by FRAC to be of special merit e.g. information on the molecular mode of resistance. Inclusion of cases of a known pathogen but a new host e.g. *Botrytis cinerea* are considered on their merits. Similarly, references reporting a known case but in a different geographical region are also considered on merit and may not be included.

Take care in using this list.

Care must be taken in using the information because:

1. Inclusion of a pathogen in this list only demonstrates that it can become resistant. It does not indicate that pathogen populations in specific geographical areas or locations are resistant. Seek local advice for specific localities. Information may also be found at the FRAC web page for specific chemical Working Groups. See www.frac.info

2. Resistance in plant pathogens can take many forms and it is important to realise the differences when consulting this list. The 'Remarks' column gives guidance on the form of resistance found and can be interpreted as:

Source: www.frac.info
January 2013

Laboratory mutation / selection: Indicates that the resistance has been selected for using various techniques including mutation by UV light, or chemical mutagenesis. Such research illustrates that resistance can happen and can provide information on the resistance mechanism, but is not a reliable indicator of the probability that resistance will happen when the chemical is used in the field.

Field trial: Indicates that resistance has been found in limited field trials. Very often such trials use application schedules that are different to commercial practice and/or are designed to pressurise pathogen populations into becoming resistant in an attempt to quantify the resistance risk. Such trials show that resistance can be generated but do not give reliable indications that resistance will occur if products are used as recommended.

Field: Indicates that resistant isolates have been found in commercially treated fields. This does not mean that the resistance was always extensive enough to cause complete disease control failure, but does indicate a need for active resistance management.

3. For pathogens capable of infecting several host genera / species e.g. *Botrytis cinerea,* the list does not include reference to all known crops. For such pathogens it is reasonable to assume that if resistance is known, all areas of use are at risk and resistance management strategies should be used.

Cross – resistance between chemicals in a particular group.

Resistance and cross-resistance between molecules in a particular group is not always absolute due to different activity spectra shown by group members. Be careful when making assumptions about cross-resistance patterns and if in any doubt refer to FRAC or the manufacturer.

A note on taxonomy

This list has been compiled using the taxonomy in use at the time the report was made. In some cases organisms have been reclassified since the original report and names have changed. Where names have changed recently, users of this list are advised to search using the old name as well as the new one.

Further guidance

Please see information published by FRAC and contained in the FRAC Monographs, available for download from the FRAC webpage www.frac.info

Source: www.frac.info
January 2013

Updates

FRAC welcomes suggestions for inclusion in this list; please send information, including full Journal reference, to the Secretary. Note that only cases of confirmed resistance will be included, supported by a published report from an accredited source. Reports of rumours of resistance or unverified reports will not be included. The decision on inclusion rests with FRAC. New entries in the 2013 edition of the list are marked in blue.

A note on mercury:
Mercury was a traditional seed treatment for cereals. It is no longer used and, as such, does not appear in the FRAC list of fungicides. Resistance did develop to it in *Pyrenophora avenae* on oats, Noble *et al.* (1966), and for *Pyrenophora graminea* on barley, Clark (1985).

Source: www.frac.info
January 2013

Mode of Action Code and Target Site	Group Name	FRAC Group Code
A: NUCLEIC ACID SYNTHESIS		
A1: RNA polymerase I	PA Fungicides Phenylamides	4
A2: Adenosine deaminase	Hydroxy – (2-amino) pyrimidines	8
A3: DNA/RNA synthesis (proposed)	Heteroaromatics	32
A4: DNA topoisomerase type II (gyrase)	Carboxylic acids	31
B: MITOSIS AND CELL DIVISION		
B1: β-tubulin assembly in mitosis	MBC fungicides, Methyl Benzimidazole Carbamates	1
B2: β-tubulin assembly in mitosis	N-phenylcarbamates	10
B3: β-tubulin assembly in mitosis	Benzamides	22
B4: Cell division (proposed)	Phenylureas	20
B5: Delocalisation of spectrin like proteins	Benzamides	43
C: RESPIRATION		
C1: Complex I, NADH oxidoreductase	Pyrimidinamines	39
C2: Complex II, succinate-dehydrogenase	SDHI fungicides	7
C3: Complex III, cytochrome bc1 (ubiquinol oxidase at Qo site (cyt b gene)	QoI fungicides, Quinone Outside Inhibitors	11
C4: Complex III, cytochrome bc1 (ubiquinone reductase) at Qi site	QiI fungicides (Quinone Inside Inhibitors)	21
C5: Uncouplers of oxidative phosphorylation	-	29
C6: Inhibitors of oxidative phosphorylation. ATP synthase	Organo tin compounds	30
C7: ATP production (proposed)	Thiophene carboxamides	38
C8: Complex III, cytochrome bc1 (ubiquinone reductase) at Qx (unknown) site	Triazolo-pyrimidylamine	45

Source: www.frac.info
January 2013

Mode of Action Code and Target Site	Group Name	FRAC Group Code
D: AMINO ACIDS AND PROTEIN SYNTHESIS		
D1: Methionine biosynthesis (proposed) (*cgs gene*)	AP fungicides. Anilinopyrimidines	9
D2: Protein synthesis	Enopyranuronic acid antibiotic	23
D3: Protein synthesis	Hexapyranosyl antibiotic	24
D4: Protein synthesis	Glucopyranosyl antibiotic	25
D5: Protein synthesis	Tetracycline antibiotic	41
E: SIGNAL TRANSDUCTION		
E1: Signal transduction (mechanism unknown)	Aza-naphthalenes	13
E2: MAP/Histidine-kinase in osmotic signal transduction (*os-2, HOG1*)	PP fungicides. Phenylpyrroles	12
E3: MAP/Histidine-kinase in osmotic signal transduction (*os-1, Daf1*)	Dicarboximides	2
F: LIPIDS AND MEMBRANE SYNTHESIS		
F1	Formerly dicarboximides	
F2: Phospholipid biosynthesis, methyl transferase	Phosphoro thiolates and dithiolanes	6
F3: Lipid peroxidation (proposed)	AH fungicides (Aromatic Hydrocarbons)(chlorophenyls, nitroanilines and heteroaromatics)	14
F4: Cell membrane permeability, fatty acids (proposed)	Carbamates	28
F5: Moved to H5	CAA fungicides. Carboxylic Acid Amides	40
F6: Microbial disrupters of pathogen cell membranes	*Bacillus subtilis* and the fungicidal lipopeptides produced	44
F7: Membrane disruption (proposed)	Plant extract	46

Source: www.frac.info
January 2013

Mode of Action Code and Target Site	Group Name	FRAC Group Code
G: STEROL BIOSYNTHESIS IN MEMBRANES		
G1: C14 demethylase in sterol biosynthesis (*erg11/cyp51*)	DMI fungicides. DeMethylation Inhibitors. SBI Class 1	3
G2: Δ^{14} reductase and $\Delta^{8} - \Delta^{7}$isomerase in sterol-biosynthesis (*erg24, erg2*)	Amines ('morpholines'). SBI class II	5
G3: 3-keto reductase, C4-demethylation (*erg27*)	Hydroxyanilides. SBI class III	17
G4: Squalene epoxidase in sterol biosynthesis (*erg1*)	SBI class IV	18
H: CELL WALL BIOSYNTHESIS		
H3: Trehalase and inositol biosynthesis	Glucopyranosyl antibiotic	26
H4: Chitin synthase	Polyoxins	19
H5: Cellulose synthase	CAA fungicides. Carboxylic Acid Amides	40
I: MELANIN SYNTHESIS IN CELL WALL		
I1: Reductase in melanin biosynthesis	MBI-R Melanin Biosynthesis Inhibitors – Reductase	16.1
I2: Dehydratase in melanin biosynthesis	MBI-D Melanin Biosynthesis Inhibitors – Dehydratase	16.2
P: HOST PLANT DEFENCE INDUCTION		
P1: Salicylic acid pathway	Benzo-thiadiazole BTH	P
P2: Benzisothiazole	Benzisothiazole	P
P3: Thiadiazole-carboxamide	Thiadiazole-carboxamide	P
P4:	Natural compound	P

Source: www.frac.info
January 2013

Mode of Action Code and Target Site	Group Name	FRAC Group Code
UNKNOWN MODE OF ACTION		
Unknown	Cyanoacetamide-oxime	27
Unknown	Phosphonates	33
Unknown	Phthalamic acids	34
Unknown	Benzotriazines	35
Unknown	Benzene-sulfonamides	36
Unknown	Pyridazinones	37
Unknown	Thiocarbamate	42
Microtubule disruption (proposed)	Thiazole carboxamide	U5
Unknown	Phenyl-acetamide	U6
Actin disruption (proposed)	Benzophenone	U8
Cell membrane disruption (proposed)	Guanidines (dodine)	U12
Unknown	Thiazolidine	U13
Unknown	Pyrimidinone-hydrazones	U14
NOT CLASSIFIED		
Unknown	Diverse	NC
MULTI-SITE CONTACT ACTIVITY		
Multi-site contact activity	Inorganic (copper)	M1
	Inorganic (sulphur)	M2
	Dithiocarbamates and relatives	M3
	Phthalimides	M4
	Chloronitriles (phthalonitriles)	M5
	Sulfamides	M6
	Guanidines	M7
	Triazines	M8
	Quinones	M9

Source: www.frac.info
January 2013

LIST OF RESISTANT PATHOGENS

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		A NUCLEIC ACID SYNTHESIS				
A1	**4**	**PA Fungicides (PhenylAmides). RNA polymerase 1**				
		Bremia lactucae	Downy mildew	Lettuce	Crute *et al.* 1987; Crute & Harrison 1988	field, genetics
		Peronospora destructor	Downy mildew	Onion	Wright 2004	-
		Peronospora hyoscyami (syn. P tabacina)	Blue mold	Tobacco	Bruck *et al.* 1982	field
		Peronospora tabacina	Blue mold	Tobacco	Bruck *et al.* 1981	field
		Peronospora viciae	Downy mildew	Pea	Falloon *et al.* 2000	field
		Phytophthora cactorum	Crown rot / leather rot	Strawberry American ginseng	Bal *et al.* 1987 Hill & Hausbeck 2008	field field
		Phytophthora capsici	Stem rot	Lima bean pods	Davey *et al.* 2008	field
		Phytophthora cinnamomi	Root rot	Avocado	Darvas & Becker 1984	field
		Phytophthora citricola	Rot / die back		Joseph & Coffey 1984	*in-vitro* mutation
		Phytophthora citrophthora	Collar rot / foot rots		Serrhini *et al.* 1985	*in-vitro*
		Phytophthora citrophthora	Collar rot / foot rots		Angeles Diaz Borras & Vila Aguila 1988	*in -vitro*
		Phytophthora erythroseptica	Pink rot	Potato	Lambert & Salas 1994 Taylor *et al.* 2002	field field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Phytophthora infestans	Late blight	Potato	Davidse *et al.* 1981 Hartill *et al.* 1983 Davidse *et al.* 1983	field field field
		Phytophthora infestans	Late blight	Poroporo	Hartill *et al.* 1983	field
		Phytophthora megasperma f.sp. glycinea	Root rot	Soybean in-vitro	Lamboy & Paxton 1992	laboratory selection
		Phytophthora megasperma f.sp. medicaginis	Root rot	Lucerne	Davidse 1981	laboratory selection
		Phytophthora melonis	Foot rot	Cucurbits	Wu *et al.* 2011	field (China)
		Phytophthora nicotianae	Root rot	Ornamentals	Hu *et al.* 2008	field
		Phytophthora palmivora	Root rot	-	Lucas *et al.* 1990	laboratory induction
		Phytophthora parasitica	Downy mildew	Periwinkle	Ferrin & Kabashima 1991	field / laboratory
		Phytophthora parasitica var. nicotianae	Black shank	Tobacco	Shew 1985	laboratory
		Phytophthora porri	Downy mildew	Leek	Locke *et al.* 1997	field
		Phytophthora sojae (syn. P megasperma)	Stem / root rot	Soybean	Bhat *et al.* 1993	laboratory
		Phytophthora sp.	Root rot	African violet	Romano & Edgington 1985	field
		Plasmopara halstedii	Downy mildew	Sunflower	Albourie *et al.* 1998	field
		Plasmopara obducens	Downy mildew	Impatiens (Busy lizzy)	FRAC 2011 FRAG UK 2011	
		Plasmopara viticola	Downy mildew	Grapevine	Staub & Sozzi 1981 Bosshard & Schuepp 1983 Leroux & Clerjeau 1985	 field field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Pseudoperonospora cubensis	Downy mildew	Cucumber	Reuveni *et al.* 1980	field
		Pythium aphanidermatum	Damping off	-	Sanders & Soika 1988	field
		Pythium aphanidermatum		Not specified / creeping bent grass	Sanders *et al.* 1990	*in-vitro* mutation / field
		Pythium aphanidermatum	Damping off	Ornamentals	Moorman *et al.* 2002	field
		Pythium cylindrosporum	Damping off	Ornamentals	Moorman *et al.* 2002	field
		Pythium dissotocum	Root rot	Carrot	White *et al.* 1988	field
		Pythium dissotocum	Root rot	Ornamentals	Moorman *et al.* 2002	field
		Pythium heterothallicum	Damping off	Ornamentals	Moorman *et al.* 2002	field
		Pythium irregular	Damping off	Ornamentals	Moorman *et al.* 2002	field
		Pythium splendens	Damping off	Ornamentals	Moorman *et al.* 2002	field
		Pythium spp.	Cavity spot various	Carrot Potato	White *et al.* 1988 Porter *et al.* 2009	field / laboratory field
		Pythium ultimum	Watery wound rot	Potato	Taylor *et al.* 2002	field
		Pythium ultimum	Damping off	Ornamentals	Moorman *et al.* 2002	field
A2	**8**	**Hydroxy (2 amino) pyrimidines: Adenosine-deaminase**				
		Erysiphe graminis f.sp. *hordei*	Powdery mildew	Barley	Hollomon 1978	field
		Sphaerotheca fuliginea	Powdery mildew	Cucurbits	Schepers 1984 O'Brien *et al.* 1988	field
A3	**32**	**Heteroaromatics DNA / RNA synthesis (proposed)** No resistance recorded				

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
A4	**31**	**Carboxylic acids**				
		Erwinia amylovora	Fire blight	Pear	Manulis *et al.* 2003, Kleitman *et al.* 2005	field survey
		B MITOSIS AND CELL DIVISION				
B1	**1**	**MBC fungicides (Methyl Benzimidazole Carbamates)**				
		Alternaria alternata	Alternaria rot	Citrus	Sitton & Pierson 1982	field
		Ascochyta byj	Ascochyta blight	Vegetables	Steekelenburg 1973	laboratory
		Ascochyta pinodes	Leaf spot	Pea	Molinero *et al.* 1993	laboratory
		Ascochyta pisi	Leaf spot	Pea	Molinero *et al.* 1993	laboratory
		Aspergillus nidulans	Bearings rot	Banana	Hasti & Georgopoulos 1971	laboratory
		Botryodiplodia theobromae	Botryodiplodia rot	Fruits (Mango)	Spalding 1982	Laboratory
		Botrytis allii	Neck rot	Onion	Viljanen-Rollinson *et al.* 2007	Field (New Zealand)
		Botrytis cinerea	Grey mold	cyclamen	Bollen & Scholten 1971	laboratory
		Botrytis cinerea	Chocolate spot	Beans	Harrison J G 1984	field
		Botrytis cinerea	Grey rot	Grapes / Vines	Ehrenhardt *et al.* 1973 Leroux *et al.* 1982 Elad *et al.* 1988	field cross resistance to phenylcarbamates, Group 10
		Botrytis cinerea	Grey mould	Lisianthus	Elad *et al.* 2008	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Botrytis elliptica	Grey rot	Lily	Chastagner & Riley 1987 Hsiang & Chastagner 1990	field
		Botrytis squamosa	Leaf blight	Alliacea	Presly & Maude1982	laboratory
		Botrytis tulipae	Fire blight	Tulip	Chastagner & Riley 1987	field
		Ceratocystis ulmi	Dutch elm disease	Elm	Brasier & Gibbs 1975	laboratory
		Cercospora apii	Early blight	Celery	Berger 1973	field
		Cercospora arachidicola	Leafspot	Peanut	Clarke *et al.* 1974; Littrell 1974	field
		Cercospora beticola	Leafspot	Sugar beet	Georgopoulos & Dovas 1973	field
		Cercospora musae	Leafspot	Banana	See *Mycosphaerella musicola*	
		Cercosporidium personatum	Late Leafspot	Peanut	Clarke *et al.* 1974	field
		Cladobotryum dendroides	Cobweb disease	Mushrooms	McKay *et al.* 1998	laboratory
		Cladosporium carpophilum	Scab	Peach, Nectarine	Chandler *et al.* 1978	field
		Cladosporium cladosporioides	Fruit rot	Fruits	Dekker 1972	review
		Cladosporium cucumerinum	Cladosporium	Cucurbits	Dekker 1972	review
		Cladosporium fulvum	Flower rot	Fruits	Staunton 1975	field
		Coccomyces hiemalis	Cherry leaf spot	Cherry	Jones & Ehret 1981	field
		Colletotrichum cereal	Anthracnose	Turfgrass	Wong *et al.* 2008	field
		Colletotrichum coffeanum	Coffee berry disease	Coffee	Cook & Pereira	field
		Colletotrichum gloeosporioides	Anthracnose	Pome fruit	Spalding 1982	laboratory
		Colletotrichum lindemuthianum	Anthracnose	Bean	Meyer 1976	review

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Colletotrichum musae	Anthracnose	Banana	Griffee 1973	field
		Corynespora cassicola	target spot	tomato	Date *et al.* 2004	field
		Cryptocline cyclaminis	Anthracnose	Cyclamen	Garibaldi *et al.* 1987	field
		Cylindrocladium scoparium	Stem canker	Eucalyptus *Callistemon* sp., *Pistacia lentiscus*	Prest &Poppe 1988 Vitale *et al.*2009	field field
		Cylindrocladium scoparium	Stem canker	Eucalyptus	Prest &Poppe 1988	field
		Didymella bryoniae	Gummy stem blight	Cucurbits	Malathrakis & Vakalounakis 1983 Steekelenburg 1987	field
		Didymella lycopersici	Stem rot	Tomato		
		Drechslera oryzae	Brown spot	Rice	Annamali & Lalithakumari 1987	laboratory
		Elsinoë fawcetti	Scab	Citrus	Whiteside 1980a Ieki 1994	field
		Elsinoë veneta	Anthracnose	Raspberry	Munro *et al.* 1988	field
		Erysiphe cichoracaerum	Powdery mildew	Cucurbits	Abelentsev & Savchenko 1980	field
		Erysiphe graminis	Powdery mildew	Cereals	Vargas 1973	field
		Erysiphe polygoni	Powdery mildew	Cowpeas	Rodriguez & Melendez 1984	field
		Erythronium spp.	Yellow fawn	Lily	Duineveld & Beijersbergen 1975	field
		Fulvia fulva also see *Cladosporium fulvum*	Leaf mold	Tomato	Miao & Higgins 1986	laboratory
		Fusarium culmorum	Fusariose	Potato / Pink	Seppanen 1983 Hanson *et al.* 1996	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Fusarium graminearum	Fusarium head blight	Cereals	Chen *et al.* 2009	Laboratory / mutation study
		Fusarium nivale	Pink snow mold	Wheat	Tanaka *et al.* 1983	field
		Fusarium oxysporium f. sp. dianthi	Fusariose	Oeillet	Tramier & Bettachini 1974	field
		Fusarium oxysporium f. sp. gladioli	Fusariose	Gladiolus	Magie & Wilfret 1974	field
		Fusarium oxysporium f. sp. lycopersici	Fusariose	Tomato	Thanassoulopoulos *et al.* 1970	laboratory
		Fusarium oxysporium f. sp. tulipae	Fusariose	Tulip	Valaskova 1983	laboratory
		Fusarium oxysporium f. sp. Melonis	Fusariose	Melon	Bastels-Schooley & MacNeil 1971	laboratory
		Fusarium roseum	Fusariose	Rosa, turf	Smiley & Howard 1976	field
		Fusarium roseum var. *sambucinum*	Dry rot	Potato	Tivoli *et al.* 1986	field
		Fusarium solani f. sp. pisi	Fusariose	Solanaceae	Richardson 1973	field, laboratory
		Fusarium sulphureum	dry rot	Potato	Hanson *et al.* 1996	field
		Fusicladium effusum	Scab	Pecan	Littrell 1977	
		Gibberella fujikuroi	Fusariose	Rice	Ogawa 1988	field
		Gibberella zeae		Rice	Liu *et al.* 2010	lab analysis
		Gloeosporium spp.	Fruit rot	Apple		
		Glomerella acutata	Storage rot	Apple	Weber & Palm 2010	field isolates
		Guignardia citricarpa	Black spot	Citrus	Herbert & Grech 1985	field
		Helminthosporium solani	Silver scurf	Potato	Geary *et al.* 2007	field (USA)
		Hypomyces rosellus	Cobweb disease	Mushrooms	Fletcher & Yarham 1976	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Leveillula taurica	Powdery mildew	Tomato	Jones & Thompson 1982	field
		Monilinia cinerea	Brown rot	Rosa	Abelentsev & Golyshin 1973	laboratory
		Monilinia fructicola	Brown rot	Pome fruit	Jones & Ehret 1976	field
		Monilinia fructigena	Brown rot	Pome fruit	Abelentsev & Golyshin 1973	laboratory
		Monilinia laxa	Brown rot	Pome fruit	Ogawa *et al.* 1981	field
		Mycogone perniciosa	Wet bubble	Mushrooms	Fletcher & Yarham 1976	field
		Mycosphaerella brassicicola	Ring spot	Brassicas		
		Mycosphaerella citri	Greasy spot	Citrus	Whiteside 1980b	field
		Mycosphaerella fijiensis	Black spot	Banana	Stover 1979	field
		Mycosphaerella fragariae	Leaf spot	Strawberry	Remiro & Kimati 1974	field
		Mycosphaerella melonis	Leaf spot / gummy stem blight	Strawberry	Kato *et al.* 1984	field
		Mycosphaerella musicola	Yellow spot	Banana	Joya C 1982	field
		Neofabraea alba	Storage rot	Apple	Weber & Palm 2010	field isolates
		Neofabraea perennans	Storage rot	Apple	Weber & Palm 2010	field isolates
		Neonectria galligena	Storage rot	Apple	Weber & Palm 2010	field isolates
		Neurospora crassa	Red mold	Bread	Sisler 1971	laboratory
		Oidiopsis taurica	Powdery mildew	Artichoke		
		Oidium begonia	Powdery mildew	Begonia		
		Penicillium brevicompactum			Bollen & Scholten 1971	laboratory

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Penicillium corymbiferum	Rot	Crocus	Bollen & Scholten 1971 Jarvis & Hargreaves 1973	laboratory field
		Penicillium digitatum	Green rot	Citrus / Pome fruit	Wild 1983	field
		Penicillium expansum	Blue mold	Pome fruit / pear	Wicks 1977	field
		Penicillium fructigenum		various	Iida W 1975	field
		Penicillium italicum	Blue rot	Citrus	Muirhead 1974; Yu 1981	field
		Penicillium oxalicum	Stem rot	Cucurbits		
		Penicillium sclerotigenum		Yellow yam	Plumbley *et al.* 1984	field
		Pestalotiopsis longiseta	Gray blight	Tea	Omatsu *et al.* 2012	field
		Pezicula alba	Ripe spot	Pome fruits	Bielenin 1986	field
		Phoma clematidina	Wilt	Clematis	*	
		Phoma tracheiphila	Malsecco	Citrus	Gilmenez & Luisi. 1978	field
		Phytophthora citricola	Dieback	Azalea	Ferrin & Kabashima 1991	field / laboratory
		Phomopsis citri	Stem-end rot	Citrus	Spalding 1982	laboratory
		Podosphaera leucotricha	Powdery mildew	Fruit trees	Suta & Radulescu 1986	laboratory
		Pseudocercosporella herpotrichoides	Eyespot	Cereals	Griffin *et al.* 1982	field
		Pyrenopeziza brassicae	Light leaf spot	Oilseed rape	Ilott *et al.* 1987	laboratory
		Rhyncosporium secalis	Leaf blotch/scald	Barley		
		Rhizoctonia solani	Brown Rhizoctonia	Solanaceae	Martin *et al.* 1984	laboratory
		Sclerotinia fructicola	Brown rot	Stone fruits	Whan J H 1976	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Sclerotinia homeocarpa	Dollar spot	Grass	Cole 1974 Detweiler *et al.* 1983 Wong S P 2003	field
		Sclerotinia sclerotorium	Sclerotiniose	Oilseed rape		
		Sclerotium spp.	Stem rot	Alliacea/Potato/Carrot		
		Septoria apiicola	Leaf spot	Celery		
		Septoria leucanthemi	Leaf spot	Chrysanthemum	Paulus *et al.* 1976	field
		Septoria tritici	Leaf spot	Cereals	Griffin & Fisher 1985	laboratory
		Sphaerotheca fuliginea	Powdery mildew	Cucurbits	Schroeder & Providenti 1971; Naegler *et al.* 1977	field
		Sphaerotheca humuli	Powdery mildew	Ornamental flowers	Iida 1975	field
		Sphaerotheca pannosa	Powdery mildew	Rosa / Peach tree	Jarvis & Slingsby 1975	field
		Sporobolomyces roseus	Pink yeast	Rosa (mutation)	Nachmias & Barash 1976	laboratory
		Stagonospora curtisii	Leaf scorch	Ornamental flowers / Narcisssus	Saniewska 1985	field
		Talaromyces flavis		Fruits	Katan *et al.* 1984	laboratory
		Tapesia yallundae	Eyespot	Cereals	see *P. herpotrichoides*	field
		Tapesia acuformis	Eyespot	Cereals	see *P. herpotrichoides*	field
		Trichoderma harzianum	Green mold	Soil / Mushrooms	Eastburn & Butler 1986	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Uncinula necator (now Erysiphe necator)	Powdery mildew	Grapes / Vines	Naegler *et al.* 1977; Pearson 1980 Pearson & Taschenberg 1980	field
		Ustilago hordei	Barley covered smut	Barley	Ben-Yephet Y *et al.* 1975	laboratory
		Venturia inaequalis	Scab	Pome fruit	Kiebacher & Hoffmann 1976	field
		Venturia nashicola	Scab	Pome fruit	Ishii & Yamaguchi 1981	field
		Venturia pirina	Scab	Pome fruit	Shabi & Ben-Yephet 1976	field
		Verticillium albo-atrum	Verticillium	Pome fruits	Ververke 1983	laboratory
		Verticillium dahlia	Verticillium	Pome fruit / Solanacea	Locke & Thorpe 1976 McHugh & Schreiber 1984	field
		Verticillium fungicola	Verticillium	Mushrooms	Fletcher & Yarham 1976; Samuels & Johnston 1980	field
		Verticillium malthousei (= V fungicola)	Verticillium	Mushrooms	Lambert & Wuest 1973	field
		Verticillium tricorpus	Wilt	Tomato		

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
B2	**10**	**N-phenyl carbamates: β tubulin assembly in mitosis**				
		Botrytis cinerea	Grey mold	Grapevine	Elad *et al.* 1988 Katan *et al.* 1989 Elad *et al.* 1992	cross resistance to phenylcarbamates, Group 10 field field
		Corynespora cassiicola	Target spot	Tomato	Date *et al.* 2004	field
		Neurospora crassa			Fujimura *et al.* 1994	resistance mechanism
		Verticillium fungicola	Dry bubble	Mushroom	Bonnen & Hopkins 1997	field isolates
B3	**22**	**Benzamides β tubulin assembly in mitosis** No resistance recorded				
B4	**20**	**Phenylureas cell division (proposed)**				
		Rhizoctonia solani	Seedling damping-off	Various vegetables and ornamentals	Chen *et al.* 1996	laboratory
B5	43	**Methyl-benzamides De-localisation of spectrin like proteins** No resistance recorded				
		C: RESPIRATION				
C1	**39**	**Pyrimidineamines: Complex 1 NADH Oxido-reductase** No resistance reported				

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
C2	**7**	**SDHI fungicides (Succinate dehydrogenase inhibitors) Complex II succinate dehydrogenase**				
		Alternaria alternata	Alternaria late blight	Pistachio	Avenot & Michallides 2007 Avenot *et al.* 2008	field resistance mechanism
		Aspergillus nidulans			White & Georgopoulos 1986	mutant study
		Coprinus cinereus			Ito *et al.* 2004	mutation study and genetic analysis
		Botryotinia fuckeliana (Botrytis cinerea)	Grey mould		Angelini *et al.* 2010	Laboratory genetic analysis
		Botrytis cinerea	Grey mould	Grapevine Strawberry Kiwi fruit Apple	FRAC 2007 FRAC 2007 Bardas *et al.*2010 Yin *et al.* 2011	field field multiple resistance field
		Botrytis elliptica	Grey mould	Lilly	FRAC 2007	field
		Corynespora cassiicola	Corynespora leaf spot	Cucumber	Miyamoto *et al.* 2007 Ishii *et al.* 2007 Miyamoto *et al.* 2009 Miyamoto *et al.* 2010b	field (greenhouses) molecular mechanism full field report field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Didymella bryoniae	Gummy stem blight	Cucurbits	FRAC 2007 Stevenson *et al.* 2008	field field
		Mycosphaerella graminicola	Leaf spot	Wheat	Skinner *et al.* 1998	laboratory mutation study
		Podosphaera xanthii	Powdery mildew	Melon Cucumber	FRAC 2007 Miyamoto *et al.* 2010a	field field (Japan, glasshouses)
		Ustilago maydis	Smut	Maize	Keon *et al.* 1991	laboratory mutation study
		Ustilago nuda	Loose smut	Barley	Leroux & Berthier 1988	field
C3	**11**	**QoI fungicides (Quinone outside Inhib.) Complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (cyt b gene)**				
		Alternaria alternata	Alternaria late blight	Pistachio	Ma *et al.* 2003 Avenot & Michallides 2007	field / laboratory field
		Alternaria alternata	Alternaria blotch	Apple	Ishii 2008	field
		Alternaria alternata	Alternaria brown spot	Citrus	Mondal *et al.* 2009	field
		Alternaria alternata	Leaf spot	Potato	FRAC 2011	field, G143A, Europe
		Alternaria arborescens	Alternaria late blight	Pistachio	Ma *et al.* 2003	field / laboratory
		Alternaria mali	Alternaria blotch	Apple	Lu *et al.* 2003	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Alternaria solani	Leaf spot	Potato	Pasche *et al.*2002, 2004, Pasche *et al*. 2005 Pasche & Gudmestad 2008	field resistance mechanism fitness of F129L
		Alternaria tenuissima	Alternaria late blight	Pistachio	Ma *et al.* 2003	field / laboratory
		Ascochyta rabiei	Ascochyta blight	Chickpea	Wise *et al.* 2009	field. Northern Great Plains / Pacific N West
		Blumeria graminis, see *Erysiphe graminis*				
		Botrytis cinerea	Grey mold	 Strawberry Strawberry, citrus Kiwi fruit	Markoglou *et al.* 2006 FRAC 2007 Ishii 2008 Bardas *et al.* 2010	mutation study Field, G143A, Germany Field, Japan Multiple resistance
		Cercospora beticola	Leaf spot	Sugar beet	Keshav Burla *et al.* 2012 Bolton *et al.* 2013	Field G143A Italy Field G143A USA
		Cercospora sojina	Frogeye spot	Soya	FRAC 2011	Field, G143A, USA
		Colletotrichum graminicola	Leaf spot	Annual bluegrass / bent grass	Avila-Adame *et al.* 2003	field
		Colletotrichum gloeosporioides	Anthracnose	Strawberry	Ishii 2008	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Corynespora cassiicola	Leaf spot, target spot	Cucumber	Ishii 2004 FRAC Brazil G143A 2012	field field
		Didymella bryoniae	Gummy stem blight	Cucurbits Watermelon	Olaya & Holm 2001 Langston 2002 Stevenson *et al.* 2002	field field field
		Didymella rabiei	Ascochyta blight	Chickpea	Gossen & Anderson 2004	field
		Erysiphe graminis tritici	Powdery mildew	Wheat	Heaney *et al.* 2000 Sierotzki *et al.* 2000a	field resistance mechanism
		Erysiphe graminis hordei	Powdery mildew	Barley	Heaney *et al.* 2000	field
		Erysiphe necator: see also *Uncinula necator*				
		Fusicladium carpophilum	Leaf spot	Almond	Foerster *et al.* 2009	California orchards
		Glomerella cingulata (Colletotrichum gloeosporioides)	Anthracnose	Strawberry	Ishii 2004	
		Magnaporthe oryzae	Leaf spot	*Lolium perenne* (perennial ryegrass)	Ma & Uddin 2009	Study on 1 field isolate
		Microdochium nivale *Microdochium majus*	Stem / head blight.	Wheat	Walker *et al.* 2009	isolates from seed
		Microdochium nivale	Head blight	Wheat	FRAC 2011	FRAC Japan report
		Microdochium spp.	Stem / head blight	CeStempeals	FRAC 2008	field, France, G143A confirmed

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Monilinia laxa *M. fructigena* *M. fructicola*	Brown rots	Fruit	Meissner & Stammler 2010	Not resistance but evidence of an intron
		Mycosphaerella fijiensis	Black Sigatoka	Banana	Heaney *et al.* 2000 Sierotzki *et al.* 2000b Chin *et al.* 2001	field resistance mechanism field
		Mycosphaerella graminicola See also *Septoria tritici*	Leaf spot	Wheat	Armand *et al.* 2003 Clark 2005 Fraaije *et al.* 2005 Gisi *et al.* 2005	field field, review field field
		Mycovellosiella nattrassii	Leaf mold	Eggplant / aubergine	Yano & Kawada 2003 Ishii 2004	field / laboratory field
		Pestalotiopsis longiseta	Gray blight	Tea	Omatsu *et al.* 2012	field
		Phaeosphaeria nodorum	Leaf blotch	Wheat	Blixt *et al.* 2009	field, molecular data
		Pseudoperonospora cubensis	Downy mildew	Cucumber	Heaney *et al.* 2000	field
		Plasmopara viticola	Downy mildew	Grapevine	Heaney *et al.* 2000 Gullino *et al.* 2004 Sierotzki *et al.* 2005	field field review
		Podosphaera fusca	Powdery mildew	Cucumber	Ishii *et al.* 2001 Fernandez-Ortuno *et al.* 2006 Fernandez-Ortuno *et al.* 2008	Field Resistance mechanism
		Podosphaera xanthii	Powdery mildew	Cucurbits	McGrath & Shishkoff 2003a, b	field trial

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Pseudoperonospora cubensis	Downy mildew	Cucumber	Heaney *et al.* 2000 Ishii *et al.* 2001	field field
		Pyrenophora teres	Net blotch	Barley	FRAC Semar *et al.* 2007	field molecular analysis (F129L)
		Pyrenophora tritici-repentis	Tan spot	Wheat	Reimann & Deising 2005 FRAC	field field
		Pyricularia grisea	Gray leaf spot	Perennial ryegrass	Vincelli & Dixon 2002 Kim *et al.* 2003	field field / resistance mechanism
		Pyricularia oryzae	Blast	Rice	FRAC Japan	field (G143A)
		Pythium aphanidermatum	Damping off	Turf	Gisi *et al.* 2002 Olaya *et al.* 2003	laboratory field / resistance mechanism
		Ramularia colli-cygni	Necrotic leaf spot	Barley	FRAC 2006	field
		Rhizoctonia solani	Sheath spot	Rice	FRAC 2011	field, F129L, USA
		Rhynchosporium secalis	Scald, leaf blotch	Barley	FRAC 2008	field, single isolate, Picardie
		Saccharomyces cerevisiae			Di Rago *et al.* 1989	resistance mechanism
		Septoria nodorum, see *Sphaeosphaeria nodorum*				
		Septoria tritici See also *Mycosphaerella graminicola*	Leaf spot	Wheat	Fraaije & Lucas 2003	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Sphaerotheca aphanis var. aphanis	Powdery mildew	Strawberry	Ishii 2008	field
		Sphaerotheca fuligenea	Powdery mildew	Cucumber	Heaney *et al.* 2000 Ishii *et al. 2001*	field field
		Stemphylium vesicarium	Brown spot	Pears	FRAC 2006 Alberoni *et al.* 2010a	field as above, field
		Stemphylium vesicarium	Purple spot / sand blast	Asparagus	FRAC 2006	field
		Uncinula necator (see also *Erysiphe necator*)	Powdery mildew	Grapevine	Wilcox *et al.* 2003	field
		Ustilago maydis	Smut	Maize	Ziogas *et al.* 2002	laboratory mutants
		Venturia inaequalis	Scab	Apple	Zheng *et al.* 2000 Farber *et al.* 2002 Steinfeld *et al.* 2002 Dux *et al.* 2005	laboratory mutants field trial field field
C4	**21**	**QiI fungicides (Quinone inside Inhibitors) Complex III cytochrome bc1 (ubiqinone reductase) at Qi site**				
		Phytophthora capsici	Stem / fruit rot	General	Kousik & Keinath 2008	Not specified
		Saccharomyces cerevisiae			Di Rago & Colson 1988	the basis of resistance
C5	**29**	**Oxidative phosphorylation uncouplers**				
		Botrytis cinerea	Grey mold	Adzuki bean	Tamura 2000	field (fluazinam)

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
C6	**30**	**Organo tin compounds Inhibitors of oxidative phosphorylation, ATP synthase**				
		Cercospora beticola	Leaf spot	Sugar beet	Giannopolitis 1978, Giannopolitis & Chrysayi-Tokousbalides M 1980	
C7	**38**	**Thiophene carboxamides ATP production (proposed)**				
		Gaeumannomyces graminis	Take-all	Wheat	Joseph-Horne *et al.* 2000 Russell *et al.* 2001 Freeman *et al.* 2005	field field / laboratory field
		D AMINO ACIDS AND PROTEIN SYNTHESIS				
D1	**9**	**AP fungicides (Anilinopyrimidines) Methionine biosynthesis (proposed) (cgs gene)**				
		Botrytis cinerea (Botryotinia fuckeliana)	Grey mold	Grapevine	Forster & Staub 1996 Chapeland *et al.* 1999 Sergeeva *et al*. 2002 Baroffio *et al.* 2003	field experiments field field field experiments
		Botrytis cinerea	Grey mould	Lisianthus	Elad *et al.* 2008	field
		Penicillium expansum	Blue mould	Apple Apple (stored prod.)	Li & Xiao 2008 Xiao *et al.* 2011	Mutation study Samples from stores

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
D2	**23**	**Enopyranuronic acid antibiotic. Protein synthesis**				
		Streptomyces lividans			Nomura *et al.* 1991	laboratory
		Pyricularia oryzae	Rice blast	Rice	Sakurai & Naito 1976	laboratory cross resistance study
D3	**24**	**Hexopyranosyl antibiotic. Protein synthesis**				
		Bacillus subtilis		Not specified	Tominaga & Kobayashi 1978	Mutation
		Pyricularia oryzae	Rice blast	Finger millet	Taga *et al.* 1979	field isolates
		Pyricularia oryzae	Rice blast	Rice	Ito & Yamaguchi 1977 Sakurai *et al.* 1977 Sakurai & Naito 1976	field field laboratory cross resistance study
D4	**25**	**Glucopyranosyl antibiotic (streptomycin). Protein synthesis**				
		Erwinia amylovora	Fire blight	Pear Pear Various Pear, apple, quince	Moller *et al.* 1972 Schroth *et al.* 1979 Basim *et al.* 2001 Manulis *et al.* 2003	field surveys
		Erwinia caratovora	Bacterial stalk rot	Maize	Chakravarti & Anilkumar 1969.	*In-vitro*
		Pseudomonas cichorii		Lettuce	Matsuzaki *et al.* 1981	field
		Pseudomonas lapsa	Bacterial stalk rot	Maize	Chakravarti & Anilkumar 1969.	*In-vitro*
		Pseudomonas syringae pv. *syringae*	Blossom blast, canker	Pear	Spotts & Cervantes 1995	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Pseudomonas syringae pv. tomato	Bacterial speck	Tomato	Silva & Lopes 1995	field
		Pseudomonas viridiflava		Lettuce	Matsuzaki *et al.* 1981	field
		Xanthomonas campestris pv. *vesicatoria*		Pepper and tomato	Minsavage *et al.* 1990	
D5	**41**	**Tetracycline antibiotic. Protein synthesis**				
		Erwinia amylovora	Fire blight	Apple, pear	Lacy *et al.* 1984 Basim *et al.* 2001	field strain selection field
		Pseudomonas syringae pv. tomato	Bacterial speck	Tomato	Silva & Lopes 1995	field
		Pseudomonas syringae pv. *syringae*	Blossom blast, canker	Pear	Spotts & Cervantes 1995	field
		E: SIGNAL TRANSDUCTION				
E1	**13**	**Aza-naphthalenes. Signal transduction, mechanism unknown**				
		Blumeria graminis f.sp. tritici *Erysiphe necator*	Powdery mildew	Wheat Grapevine	Genet & Jaworska 2009	Baseline, cross resistance studies
		Erysiphe graminis f. sp. *hordei*	Powdery mildew	Barley	Hollomon *et al.* 1997	mutation
E2	**12**	**PP fungicides (Phenylpyrroles). MAP / Histidine-kinase in osmotic signal transduction (os-2, HOG1)**				
		Alternaria brassicicola	Leaf spot	Brassicas	Avenot *et al.* 2005	field / laboratory resistance mechanism

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Aspergillus parasiticus		Artificial media	Markoglou *et al.* 2008	mutation study
		Botryotinia fuckeliana	Grey mold	Grapevine	Faretra & Pallastro 1993	mutation
		Fusarium spp.	Seed piece decay	Potato	Peters *et al.* 2008	Not specified
		Penicillium digitatum	Green mould	Not specified	Kanetis *et al.* 2008	Isolates from packing houses but no crop losses
		Penicillium expansum	Blue mould	Apple	Li & Xiao 2008	Mutation study
E3	**2**	**Dicarboximides. MAP / Histidine-kinase in osmotic signal transduction (os-1, Daf1)**				
		Alternaria alternata	Leaf spot	Passion fruit	Hutton D G	laboratory / field
		Alternaria spp. *alternata, tenuissima, arborescens* group	late blight	Pistachio	Ma & Michailides 2004	field / induced
		Alternaria brassicicola	Leaf spot	Brassicas	Avenot *et al.* 2005	field / laboratory resistance mechanism
		Alternaria daucii	Leaf spot / blight	Carrot	Strandberg 1984 Fancelli & Kimati 1991	laboratory
		Botryosphaeria dothidea	Panicle / shoot blight	Pistachio	Ma *et al.* 2001	laboratory / field
		Botrytis cinerea	Grey mold	Cucumber	Steekelenburg 1987	field
		Botrytis cinerea	Grey mold	Grapevine	Holz 1979 Leroux *et al.* 1982	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Botrytis cinerea	Grey mold	Strawberry	Davis & Dennis 1979	field
		Botrytis cinerea	Grey mould	Lisianthus	Elad *et al.* 2008	field
		Botrytis elliptica	Grey mold	Bulbs	Hsiang & Chastener 1990	field
		Botrytis squamosa	Leaf blight	Onion	Tremblay *et al.* 2003	laboratory
		Botrytis tulipae	Tulip fire	Tulip	Chastagner & Riley 1987	field
		Didymella bryoniae	Grey mold	Cucumber	Steekelenburg 1987	field
		Microdochium nivale	Snow mold	Grass / golf course	Pennucci *et al.* 1990	field
		Monilinia fructicola	Brown rot / twig/ blossom blight	Stone fruit	Penrose *et al.* 1985 Elmer & Gaunt 1994	field
		Monilinia laxa	Brown rot	Apple	Katan & Shabi 1981	laboratory
		Neurospora crassa			Grindle 1984	laboratory mutation
		Pyrenopeziza brassicae	Light leaf spot	Oilseed rape / brassicas	Ilott & Ingram 1987	laboratory selection / mutation
		Sclerotinia homeocarpa	Dollar spot	*Agrostis palustris* (bent grass)	Detweiler *et al.* 1983	field
		Sclerotinia minor	Basal rot	Lettuce	Hubbard *et al.* 1997	field
		Sclerotinia minor	Sclerotinia blight	Peanut	Brenneman *et al.* 1987 Smith *et al.* 1995	laboratory field
		Stemphylium vesicarium	Brown spot	Pear	Alberoni *et al.* 2005 Alberoni *et al.* 2010b	field Resistance mechanism

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Ustilago maydis	Smut	Maize	Orth *et al.* 1994	laboratory mutation
		F LIPIDS AND MEMBRANE SYNTHESIS				
F1	Formerly dicarbox-imides	Reclassified into E3				
F2	**6**	**Phosphoro-thiolates and dithiolanes. Phospholipid biosynthesis, methyltransferase**				
		Bipolaris oryzae	Rice	Rice blast	Annamalai & Lalithakumari 1992	mutagenisis and field
		Pyricularia oryzae	Rice	Rice blast	Uesugi 1981	mutation and field
F3	**14**	**AH fungicides (Aromatic Hydrocarbons, chlorophenyls, nitroanilines, and heteroaromatics). Lipid peroxidation (proposed)**				
		Botrytis cinerea	Grey mold	Glasshouse vegetables	Esuruoso & Wood 1971 Hartill *et al.* 1983	laboratory / field cross resistance studies with dicarboximides, Group 2
		Phytophthora drechsleti	-	-	Zhu Zhi-feng *et al.* 2006	Laboratory UV mutation, etridiazole

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Rhizoctonia solani	-	-	Anilkumar & Pandourange Gowda 1981 Van Bruggen & Arneson 1984	PCNB *in-vitro* adaptation Tolclofos-methyl, *in-vitro* adaptation
		Sclerotium rolfsii	Southern blight / stem rot	Peanut	Shim *et al.* 1998	field
F4	**28**	**Carbamates. Cell membrane permeability, fatty acids (proposed)**				
		Pythium spp. (propamocarb) *P. aphanidermatum* *P cylindrosporium* *P. dissotocum* *P heterothalicum group F* *P. irregulare* *P. splendens* *P. ultimum*	Damping off	Not specific but tested on geranium seedlings	Moorman et al. 2002, Moorman and Kim 2004	Glasshouse isolates
		G: STEROL BIOSYNTHESIS IN MEMBRANES				
G1	**3**	**DMI Fungicides (DeMethylation Inhibitors) SBI Class I. C14-demethylase in sterol biosynthesis (*erg11 / cyp 51)***				
	IMPORTANT NOTE: The DMI group includes several areas of chemistry (See FRAC Code List) and many molecules. Individual molecules can differ widely in their activity spectrum. Cases are known where resistance to one molecule does not always lead to resistance to another molecule. Reasons for this phenomenon are not always clear but appear to be linked to differences in the intrinsic levels of activity between molecules. If in any doubt assume that cross resistance can happen.					
		Aspergillus nidulans	-	-	De Waard & van Nistelrooy 1979	genetic study
		Blumeriella jaapii	Leaf spot	Cherry	Proffer *et al.* 2006	field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Botrytis cinerea	Grey mold	Vegetables Various	Elad 1992 Stehmann & De Waard 1996	field laboratory investigation of lack of intrinsic activity
		Cercospora beticola	Leaf spot	Sugar beet	Henry & Trivellas 1989 Karaoglanidis *et al.* 2000	Laboratory mutants Field isolates
		Cladosporium caryigenum	Scab	Pecan	Reynolds et al. 1997	cross resistance, laboratory
		Colletotrichum gloeosporioides	Anthracnose	Mango	Gutierrez-Alonso et al. 2003	postharvest / laboratory
		Erysiphe graminis f .sp. hordei	Powdery mildew	Barley	Fletcher & Wolfe 1981	field
		Erysiphe graminis f .sp. tritici	Powdery mildew	Wheat	De Waard et al. 1986	field
		Fusarium asiaticum *Fusarium graminearum*	Fusarium head blight	Wheat	Yin et al. 2009	Lab study on isolates from China
		Fusarium fujikuroi	-	-	Zhao Zhi-hua et al. 2007	Laboratory mutation (prochloraz)
		Fusarium solani. See Nectria haematococca var. *cucurbiae*	Cucurbits	Foot rot	Kalamarakis *et al.* 1991	genetic study
		Microdochium (Fusarium) nivale	-	-	Cristani & Gambogi 1993	Laboratory
		Monilinia fructicola	Twig blight, brown rot	Stone fruit	Nuninger-Ney *et al.* 1989	Laboratory Field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
					Elmer *et al.* 1992	
		Mycosphaerella fijiensis	Sigatoka	Banana	Anonymous 1992	
		Mycosphaerella graminicola	Leaf spot	Wheat	Metcalfe *et al.* 2000 Mavroedi & Shaw 2005 HGCA 2005 Cools *et al.* 2005	field experiments field experiments field laboratory
		Mycovellosiella nattrassii	Leaf mold	Eggplant	Yamaguchi *et al.* 2000	field
		Nectria haematococca var. *cucurbiae*	Cucurbits	Foot rot	Kalamarakis *et al.* 1991	laboratory genetics
		Penicillium digitatum	Citrus	Green mold	Eckert 1987	Laboratory selection
		Penicillium italicum	-	Blue mold	De Waard *et al.* 1982	laboratory
		Pseudocercosporella herpotrichoides Lente or R type	Eyespot	Wheat	Leroux & Marchegay 1991	field
		Puccinia horiana	White rust	Chrysanthemum	Cevat 1992 Cook 2001	field field
		Puccinia striiformis	Yellow / stripe rust	Wheat	Bayles *et al.* 2000 Napier *et al.* 2000	sensitivity shift laboratory
		Pyrenophora teres	Net blotch	Barley	Sheridan *et al.* 1985	field
		Pyrenophora tritici-repentis	Tan spot	Wheat	Reimann & Deising 2005	field
		Rhynchosporium secalis	Leaf blotch, scald	Barley	Hunter *et al.* 1986 Kendall & Hollomon 1990 Kendall *et al.* 1993 Cooke *et al.* 2004	Glasshouse field Field isolates field

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Sclerotinia homoeocarpa	-	-	Vargas *et al.* 1992	laboratory
		Septoria tritici				See *Mycosphaerella graminicola*
		Sphaerotheca fuligenea	Powdery mildew	Cucumber	Schepers 1983, 1985a, 1985b	field
		Sphaerotheca mors-uvae	Powdery mildew	Blackcurrant	Goszczynski *et al.* 1988	field
		Sphaerotheca pannosa	Powdery mildew	Nectarine	Reuveni 2001	field
		Trichoderma koningii	-	-	Figueras-Roca *et al.* 1996	Laboratory
		Uncinula necator	Powdery mildew	Grapevine	Steva *et al.* 1990 Reidi & Steinkellner 1996 Miller & Gubler 2003	field field field
		Ustilago avenae	Loose smut	Oats	Hippe & Koller 1986	laboratory
		Ustilago maydis	Smut / blister smut	Maize	Walsh & Sisler 1981	laboratory
		Venturia inaequalis	Scab	Apple	Stanis & Jones 1985; Köller *et al.* 1991	field laboratory
		Venturia nashicola	Japanese pear scab	Pear	Tomita & Ishii 1998	field
G2	**5**	**Amines (Morpholines) SBI Class II. Δ^{14} reductase and $\Delta^{8} – \Delta^{7}$ isomerase in sterol biosynthesis (*erg24 / erg2*)**				
		Erysiphe graminis tritici	Powdery mildew	Wheat	Napier *et al.* 2000	sensitivity shift

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Erysiphe graminis hordei	Powdery mildew	Barley	Napier *et al.* 2000	sensitivity shift
		Nectria haematococca			Lasseron-De Felandre *et al.* 1999	laboratory mutants
		Ustilago maydis	Smut	Maize	Markoglou & Ziogas 1999, 2000, 2001	laboratory mutants
G3	**17**	**Hydroxyanilides (SBI class III). 3-keto reductase C4-demethylation *(erg27)***				
		Botrytis cinerea (Botryotinia fuckeliana)	Grey mold	Grapevine	Baroffio *et al.* 2003 Ziogas *et al.* 2003 Saito *et al.* 2011	field experiments mutants field (New York)
		Botrytis cinerea	Grey mould	Lisianthus	Elad *et al.* 2008	field (low frequency)
G4	**18**	**SBI Class IV. Squalene epoxidase in sterol biosynthesis (*erg1)*** No resistance recorded				
		H: GLUCAN SYNTHESIS				
H3	**26**	**Glucopyranosyl antibiotic (validamycin). Trehalase and inositol biosynthesis**				
		Coprinus cinereus			Shim *et al.* 1994	
H4	**19**	**Polyoxins. Chitin synthase**				
		Cochliobolus heterostrophus			Gafur *et al.* 1998	laboratory mutation
		Alternaria alternata	Black leaf spot	Pear	Gasonshi & Takanashi	

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Alternaria kikuchiana	Alternaria leaf blotch	Apple, pear	Hori *et al.* 1976	laboratory study on resistance mechanism
		Alternaria mali	Black leaf spot	Apple	Hwang & Yun 1986	field isolates
		Alternaria solani		Not specified	Maria & Sullia 1986	laboratory adaptation study
		Sclerotium rolfsii		Not specified	Maria & Sullia 1986	laboratory adaptation study
H5	**40**	**CAA fungicides (Carboxylic acid amides). Cellulose synthase**				
		Phytophthora capsici	Stem and fruit rot	Peppers	Young *et al.* 2001 Young *et al.* 2005 Lu *et al.* 2010	laboratory selection cross resistance study field
		Phytophthora infestans	Late blight	Potato	Dereviagina *et al.* 1999 Stein & Kirk 2003 Yuan *et al.* 2006	unstable field isolates mutation mutation
		Phytophthora melonis	Foot rot	Cucumber/cucurbits	Lei Chen *et al.* 2012	mutation
		Phytophthora parasitica	Black shank	Tobacco	Chabane *et al.* 1993	mutation
		Plasmopara viticola *Pseudoperonospora cubensis*	Downy mildew Downy mildew	Vines Cucurbits	Gisi *et al.* 2007 Blum *et al.* 2010 Blum *et al.* 2011	inheritance of resistance resistance mechanism resistance mechanism

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		I: MELANIN SYNTHESIS IN CELL WALL				
I1	**16.1**	**MBI-R (Melanin biosynthesis Inhibitors: Reductase). Reductase in melanin biosynthesis**				
		Magnaporthe grisea / Pyricularia oryzae	Rice blast	Rice	Zhang *et al.* 2006	UV light generated mutants
I2	**16.2**	**MBI-D (Melanin biosynthesis Inhibitors: Dehydratase). Dehydratase in melanin biosynthesis**				
		Magnaporthe grisea / Pyricularia oryzae	Rice blast	Rice	Yamaguchi *et al.*2002 Sawada *et al.* 2004 Takagaki *et al.* 2004 Yamada *et al.* 2004	Field field resistance mechanism field
		P: HOST PLANT DEFENCE INDUCTION				
P1	**P**	**Benzo-thiadiazole BTH. Salicylic acid pathway** No resistance recorded				
P2	**P**	**Benzisothiazole** No resistance recorded				
P3	**P**	**Thiadiazole-carboxamide** No resistance recorded				
P4	**P**	**Natural compound (Laminarin)** No resistance recorded				

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		U: UNKNOWN MODE OF ACTION				
U	**27**	**Cyanoacetamide oximes**				
		Plasmopara viticola	Downy mildew	Grapevine	Gullino *et al.* 1997	field
U	**33**	**Phosphonates**				
		Bremia lactucae	Downy mildew	lettuce	Brown *et al.* 2004	field
		Phytophthora citrophthora	Collar rot / foot rots		Angeles Diaz Borras & Vila Aguila 1988	*in -vitro*
		Plasmopara viticola	Downy mildew	Grape vine	Khilare *et al.* 2003	field
		Pythium aphanidermatum		Not specified	Sanders *et al.* 1990	*in-vitro* mutation
U	**34**	**Phthalamic acids** No resistance recorded				
U	**35**	**Benzotriazines** No resistance recorded				
U	**36**	**Benzene-sulfonamides** No resistance recorded				
U	**37**	**Pyradazinones** No resistance recorded				
U	**42**	**Thiocarbamate** No resistance recorded				
U	**U5**	**Thiazole carboxamides. Microtubule disruption (proposed)** No resistance recorded				
U	**U6**	**Phenyl-acetamide**				
		Sphaerotheca cucurbitae	Powdery mildew	Cucumber	Hosokawa *et al.* 2006	glasshouses, Japan

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
U	**U7**	**Cancelled: See E1**				
Actin disruption (proposed)	**U8**	**Benzophenone**				
		Blumeria graminis	Powdery mildew	wheat	Top Agrar, Dec. 2009 Felsenstein *et al.* 2010 (as above)	field, Germany field, Germany
U	**U10**	**Acrylonitrile** No resistance recorded				
		NC: NOT CLASSIFIED				
Not known	**diverse**	**Various mineral oils, organic oils, potassium bicarbonate, material of biological origin.**				
		Botryotinia fuckeliana	Resistant to *Bacillus subtilis* strain CL27		Li & Leifert 1994	Lab study
		M: MULTISITE CONTACT ACTIVITY				
	M1	**Inorganics, copper**				
		Pseudomonas species*:* *P. cepacia* *P. gladioli* *P. syringae pv. actinidiae* *Agrobacterium* species*:* *A. radiobacter* *A. tumefaciens*		Not specified, laboratory isolates	Goto *et al.* 1994	*in-vitro* tests

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Xanthomonas axonopodis pv. *citri*	Citrus canker	Grapefruit	Canteros 2002	Field
	M2	**Inorganics, sulphur** No resistance recorded				
	M3	**Dithiocarbamates and relatives**				
		Botrytis cinerea	Grey mold	Not specified	Barak & Edgington 1984	laboratory study
		Helminthosporium halodes	Leaf spot	Sugar cane	Reddy & Anilkumar 1989	laboratory study
	M4	**Phthalimides**				
		Botrytis cinerea	Grey mold	Not specified	Barak & Edgington 1984	laboratory study
		Botrytis cinerea		Grapevine	Fourie & Holz 2001	laboratory
		Botrytis cinerea	Grey mold	Glasshouse cucumber	Malathrakis 1989	glasshouse
	M5	**Chloronitriles (phthalonitriles)**				
		Botrytis cinerea	Grey mold	Not specified	Barak & Edgington 1984	laboratory study
		Botrytis cinerea	Grey mold	Glasshouse cucumber	Malathrakis 1989	
	M6	**Sulphamides**				
		Botrytis cinerea	Grey mold	Glasshouse cucumber	Malathrakis 1989	
	M7	**Guanidines**				
		Venturia inaequalis	Scab	Apple	Szkolnik & Gilpatrick 1969, 1971	Dodine
		Hypomyces	-	-	Kappas & Georgopoulos	Dodine, induced resistance

Source: www.frac.info
January 2013

MOA Code	FRAC Group Code	Pathogen	Common name	Crop	Reference	Remarks
		Penicillium digitatum	Green mold	Citrus	Wild 1983	
		Penicillium italicum	Blue mold	Lemon	Hartill *et al.* 1983	*in-vitro*
	M8	**Triazines** No resistance recorded				

Source: www.frac.info
January 2013

References

A

Alberoni G, Cavallini D, Collina M, Brunelli A (2010a) Characterisation of the first *Stemphylium vesicarium* isolates resistant to strobilurins in Italian pear orchards. *European Journal of Plant Pathology* **126** 453-457

Alberoni G, Collina M, Lanan C, Leroux P, Brunelli A (2010b). Field strains of *Stemphylium vesicarium* with a resistance to dicarboximide fungicides correlated with changes in a two-component histidine kinase. *European Journal of Plant Pathology* **128,** 171-184

Angeles Diaz Borras M, Vila Aguilar R (1988). In-vitro resistance of *Phytophthora citrophthora* to metalaxyl and fosetyl-Al.

Anonymous (1992). Sterol biosynthesis inhibitors – risk of resistance and recommended antiresistance strategies. Recommendations of the FRAC-DMI Working Group for 1992. *Gesunde Pflanzen* **44,** 361 – 365

Abelentsev V I, Golyshin N M (1973). Adaptatsiya nekotorykh fitopatogennykh gribov k benomilu. *Kimila v Sel'skom Khoz* **11,** 432-436

Abelentsev V I, Savchenko V I (1980). Resistance of the causative agent of powdery mildew of cucumbers to benzimidazole fungicides. *Khimiya v Sel'skrom Khozyaistve* **18,** 31 - 33

Alberoni G, Collina M, Pancaldi D, Brunelli A (2005). Resistance to dicarboximide fungicides in *Stemphylium vesicarium* of Italian pear orchards. *European Journal of Plant Pathology* **113,** 211-219

Albourie J-M, Tourville J, Tourviellie De Labrouhe D (1998). Resistance to metalaxyl in isolates of the sunflower pathogen *Plasmopara halstedii*. *European Journal of Plant Pathology* **194,** 235 – 242

Amand O, Calay F, Coquillart L, Legat T, Bodson B, Moreau J-M, Maraite H (2003). First detection of resistance to QoI fungicides in *Mycosphaerella graminicola* on winter wheat in Belgium. *Communications in Agricultural and Applied Biological Sciences* **68,** 519-531

Angelini R M C, Habib W, Rotolo C, Pollastro S, Faretra F (2010). Selection, characterisation and genetic analysis of laboratory mutants of *Botryotinia fuckeliana* (*Botrytis cinerea*) resistant to the fungicide Boscalid. *European Journal of Plant Pathology* **128**, 185-199

Anilkumar T B, Pandourange Gowda K T (1981). Growth and stability of penta chloronitro benzene resistant isolate of *Rhizoctonia solani. Zentralblatt fuer Bakteriologie Parasitenkunde Infektionskrankheiten und Hygiene Zweite Naturwissenschaftliche Abteilung Mikrobiologie der Landwirtschaft der TEchnologie und des Umweltschutzes* **136,** 502-504

Annamalai P, Lalithakumari D (1987). Cross resistance in edifenphos resistant mutant of *Dreschlera oryzae. Indian Phytopathology* **40,** 296

Annamalai P, Lalithakumari D (1992). Development of resistance in *Bipolaris oryzae* against edifenphos. *Mycological Research* **96,** 454-460

Avenot H, Simoneau P, Iacomi-Vasilescu B, Bataille-Simoneau N (2005). Characterisation of mutations in the two component histidine kinase gene AbNIK1 from *Alternaria brassicicola* that confer high dicarboximide and phenylpyrrole resistance. *Current Genetics* **47,** 234-243

Avenot H F, Michallides T J (2007). Resistance to pyraclostrobin, boscalid and Pristine (pyraclostrobin plus boscalid) in *Alternaria alternate* isolates from California. *Phytopathology* **97**, (7, Suppl. S) S5 Jul 2007.

Avenot H F, SellamA, Karaoglanidis G, Michailides T J (2008). Characterization of mutations in the iron-sulphur subunit of succinate dehydrogenase correlating with boscalid resistance in *Alternaria alternata* from California pistachio. *Phytopatholgy* **98**, 736-742

Source: www.frac.info
January 2013

Avila-Adame C, Olaya G, Koller, W (2003). Characterisation of *Colletotrichum graminicola* isolates resistant to strobilurin related QoI fungicides. *Plant Disease* **87,** 1426-1432

B

Bal E, Gilles G, Creemers P, Vandergeten-Bollen J (1987). *Mededelingen van de Faculteit Landbouwwetenschappen Universiteit Gent* **52,** 881 – 894

Barak E, Edgington L V (1984). Cross resistance of *Botrytis cinerea* to captan, thiram, chlorothalonil and related fungicides. *Canadian Journal of Plant Pathology* **6,** 318-320

Bardas G A, Veloukas T, Koutita O, Karaoglanidis G S (2010). Multiple resistance of *Botrytis cinerea* from kiwi fruit to SDHIs, QoIs and fungicides of other chemical groups. *Pest Management Science* **66**, 967-973

Baroffio C A, Siegfried W, Hilber U W (2003). Long-term monitoring for resistance of *Botryotinia fuckeliana* to anilinopyrimidine, phenylpyrrole and hydroxyanilide fungicides in Switzerland. *Plant Disease* **87,** 662-666

Basim H, Ozturk S B, Unlu A, Yegen O, Zeller W (2001). Evaluation of *Erwinia amylovora* strains in Turkey for resistance to streptomycin, oxytetracycline and copper. *Phytopathology* **91,** S6

Bastels-Schooley J, MacNeil B H (1971). A comparison of the mode of action of three benzimidazoles. *Phytopathology* **61,** 816-819

Bayles R A, Stigwood P L, Clarkson J D S (2000). Shifts in sensitivity of *Puccinia striiformis* to DMI fungicides in the UK. *Acta Phytopathologica et Entomologica Hungarica* **35,** 381 - 382

Ben-Yephet Y, Henis Y, Dinoor A (1975). Inheritance of tolerance to carboxin and benomyl in *Ustilago hordei. Phytopathology* **65,** 563 – 567

Berger R D (1973). Disease progress of *Cercospora apii* resistant to benomyl. *Plant Disease Reporter* **57,** 837 - 840

Bhat R G, McBlain B A, Schmitthenner A F (1993). The inheritance of resistance to metalaxyl and to fluorophenylalanine in mating of homothallic *Phytophthora sojae. Mycological Research* **97,** 865 – 870

Bielenin A (1986). Resistance to benzimidazole fungicides in *Pezicula* spp. *Ochr. Rosl.* **30,** 16-17

Blixt E, Djurle A, Yuen J, Olson Å (2009). Fungicide sensitivity in Swedish isolates of *Phaeosphaeria nodorum*. *Plant Pathology* **58**, 655-664

Blum M, Waldner M, Gisi U (2010). A single point mutation in the novel PvCesA3 gene confers resistance to the carboxylic acid amide fungicide mandipropamid in *Plasmopara viticola. Fungal Genetics and Biology*. **47,** 499-510

Blum M, Waldner M, Olaya G, Cohen Y, Gisi U, Sierotzki H (2011). Resistance mechanism to carboxylic acid amide fungicides in the cucurbit downy mildew pathogen *Pseudoperonospora cubensis. Pest Management Science,* **67,** 1211-1214

Bollen G J, Scholten G (1971). Acquired resistance to benomyl and some other systemic fungicides in a strain of *Botrytis cinerea* in cyclamen. *Netherlands Journal of Plant Pathology* **77**, 83 – 90

Bonnen A M, Hopkins C (1997). Fungicide resistance and population variation in *Verticillium fungicola*, a pathogen of the button mushroom, *Agaricus bisporus. Mycological Research* **101,** 89-96

Bosshard E, Schuepp H (1983). Variability of selected strains of *Plasmopara viticola* with respect to their metalaxyl sensitivity under field conditions. *Zeitschrift fuer Pflanzenkrankheiten und Pflanzenschutz* **90,** 449 – 459

Source: www.frac.info
January 2013

Brasier C M, Gibbs J N (1975) Methyl benzimidazole-2-yl carbamate tolerance in aggressive and nonaggressive isolates of *Ceratocystis ulmi. Annals of Applied Biology* **80,** 231 – 236

Brenneman T B, Phipps P M, Stipes R J (1987). Sclerotinia blight of peanut relationship between *in vitro* resistance and field efficacy of dicarboximide fungicides. *Phytopathology* **77,** 1028-1032

Brown S, Koike S T, Ochoa O E, Laemmien F, Michelmore R W (2004). Insensitivity to the fungicide fosetyl-aluminum in California isolates of the lettuce downy mildew pathogen *Bremia lactucae*. *Plant Disease* **88,** 502-508

Bruck R, Gooding G V Jr, Main C E (1981). Evidence for resistance to metalaxyl in isolates of *Peronospora tabacina. Phytopathology* **71**, 558

Bruck R, Gooding G V Jr, Main C E (1982). Evidence for resistance to metalaxyl in isolates of *Peronospora hyoscyami. Plant Disease* **66**, 44 – 45

C

Canteros B (2002). Control of citrus canker caused by strains of *Xanthomonas axonopodis* pv. *citri* susceptible and resistant to copper. *Phytopathology* **92,** S116 (meeting abstract)

Cevat H (1992). Japanse roest terug van nooit weggeweest. nu maatregelen nemen om aantasting in najaar te voorkomen. *Vakblad voor de Bloemisterij* **29,** 32 – 33

Chabane K, Leroux P, Bompeix G (1993). Selection and characterisation of *Phytophthora parasitica* mutants with ultraviolet induced resistance to dimethomorph or metalaxyl. *Pesticide Science* **39,** 325-329

Chakravarti B P, Anilkumar T B (1969). *Hindustan Antibiotics Bulletin* **12,** 73-74

Chandler W A, Daniell J W, Littrell R H (1978). Control of peach diseases in annorchard having benomyl tolerant *Cladosporium carpophilum. Plant Disease Reporter* **62,** 783 – 786

Chapeland F, Fritz R, Lanen C, Gredt M, Leroux P (1999). Inheritance and mechanisms of resistance to anilinopyrimidine fungicides in *Botrytis cinerea* (*Botryotinia fuckeliana). Pesticide Biochemistry and Physiology* **64,** 85-100

Chastagner G A, Riley K (1987). Occurrence and control of benzimidazole and dicarboximide resistant *Botrytis* spp. on bulb crops in Western Washington and Oregon USA. *Phytopathology* **77,** 1237

Chen Y R, Huang J W, Chen L C (1996). In vitro inspection of pencycuron fungicide: Resistant *Rhizoctonia solani* Ag-4 and its interfering factors. *Plant Protection Bulletin (Taichung)* **38,** 313-328

Chen Yu, Zhou Ming-Guo (2009). Characterization of *Fusarium graminearum* isolates resistant to both carbendazim and a new fungicide JS399-19. *Phytopathology* **99** 441

Chin K M, Wirz M, Laird D (2001). Sensitivity of *Mycosphaerella fijiensis* from banana to trifloxystrobin. *Plant Disease* **85, 1264-1270**

Clark E M, Backman P A, Rodriguez-Kabana R (1974). *Cercospora arachidicola* and *Cercosporidium personatum* tolerance to benomyl and related fungicides in Alabama peanut fields. *Phytopathology* **64,** 1476 – 1477

Source: www.frac.info
January 2013

Clark M R M (1985). Barley leaf stripe mercury resistance. In: *British Crop Protection Council Monograph No. 31. Fungicides for Crop Protection: 100 Years of Progress, Vol 2, Bordeaux Mixture Centenary Meeting.* BCPC Publications, Croydon, England. pp. 351-354

Clark W (2005). QoI resistance in *Mycosphaerella graminicola* in the UK: implications for future use of QoI fungicides. *Proceedings of the BCPC International Congress, Crop Science & Technology* 283-290

Cole H, Warren C G, Sanders P L (1974). Fungicide tolerance – a rapidly emerging problem in turfgrass disease control. *Proceedings International Turfgrass Research Conference.* **2D,** 344-349

Cook R T A, Pereira J L (1976). Strains of *Colletotrichum coffeanum* the causal agent of coffee berry disease tolerant to benzimidazole compounds in Kenya. *Annals of Applied Biology* **83,** 365 – 379

Cooke L, Locke T, Lockley K D, Phillips A N, Sadiq M D S, Coll R, Black L, Taggart P J, Mercer P C (2004). The effect of fungicide programmes based on epoxyconazole on the control and DMI sensitivity of *Rhynchosporium secalis* in winter barley. *Crop Protection* **23,** 393-406.

Cools H J, Fraaje B A, Lucas J A (2005). Molecular mechanisms correlated with changes in triazole sensitivity in isolates of *Mycosphaerella graminicola*. *Proceedings of the BCPC International Congress, Crop Science & Technology 2005,* 267-274

Cristani C, Gambogi P (1993). Laboratory isolation of *Microdochium (Fusarium) nivale* mutants showing reduced sensitivity to sterol biosynthesis inhibitors. *Rivista di Patalogia Vegetale* **3,** 49 - 57

Crute I R, Norwood J M, Gordon P L (1987). The occurrence, characteristics and distribution in the United Kingdom of resistance to phenylamide fungicides in *Bremia lactucae* (lettuce downy mildew). *Plant Pathology* **36,** 297 - 315

Crute I, Harrison J M (1988). Studies on the inheritance of resistance to metalaxyl in *Bremia lactucae* and on the stability and fitness of field isolates. *Plant Pathology* **37,** 231 – 250

D

Darvas J M, Becker O (1984). Failure to control *Phytophthora cinnamomi* and *Pythium splendens* with metalaxyl after its prolonged use. *Citrus and Subtropical Fruit Journal* **603**, 9 – 11.

Date H, Kataoka E, Tanina K, Sasaki S, Inoue K, Nasu H, Kasuyama S (2004). Sensitivity of *Corynespora cassicola*, causal agent of Corynespora target spot of tomato, to thiophanate methyl and diethofencarb.*Japanese Journal of Phytopathology* **70,** 7-9

Davey J F, Gregory N F, Mulrooney R P, Evans T A, Carroll RB (2008). First report of mefenoxam resistant isolates of *Phytophthora capsici* from lima bean pods in the Mid-Atlantic region. Plant Disease **92**, 656

Davidse L C (1981). Resistance to acylalanine fungicides in *Phytophthora megasperma* f. sp. *medicaginis. The Netherlands Journal of Plant Pathology* **87,** 11-24

Davidse L C, looijeu D, Turkenstein L J, Van Der Wal D (1981). Occurence of metalaxyl resistant strains of potato blight in Dutch potato fields. *The Netherlands Journal of Plant Pathology* **87,** 65 - 68

Davidse L C, Danial D L, Van Westen C J (1983). Resistance to metalaxyl in *Phytophthora infestans* in the Netherlands. *The Netherlands Journal of Plant Pathology* **89,** 1 – 20

Source: www.frac.info
January 2013

Davis R P, Dennis C (1979). Use of dicarboximide fungicides on strawberries and potential problems of resistance in *Botrytis cinerea. Proceedings of the British Crop Protection Conference, Pests & Diseases* 193 – 201

De Waard M A, Van Nistelrooy J G M (1979). Mechanisms of resistance to fenarimol in *Aspergillus nidulans. Pesticide Biochemistry and Physiology* **10,** 219 – 229

De Waard M A, Groeneweg H, Van Nistelrooy J G M (1982). Laboratory resistance to fungicides which inhibit ergosterol biosynthesis in *Penicillium italicum. Netherlands Journal of Plant Pathology* **88,** 99 – 112

De Waard M A, Kipp E M C, Horn N M, Van Nistelrooy J G M (1986). Variation in sensitivity to fungicides which inhibit ergosterol biosynthesis in wheat powdery mildew. *Netherlands Journal of Plant Pathology* **92,** 21 – 32

Dekker J (1972) In: Marsh R W, *Systemic Fungicides.* John Wiley & Son, New York. pp 156-174

Derevyagiana M K, Matskavichus G, D'Yakov Yu T (1995). Changes of resistance to dimethomorph of *Phytophthora infestans* (Mont.) D By. isolates during cloning. *Mikologiya i Fitopatologiya* **29,** 44-47

Dereviagina M K, Elanski S N, Diakov Yu T (1999). Resistance of *Phytophthora infestans* to the dimethomorph fungicide. *Mikologiya i Fitopatologiya* **33,** 208-213

Detweiler A R, Yargas J M Jr., Danneberger T K (1983). Resistance of *Sclerotinia homoeocarpa* to iprodione and benomyl. *Plant Disease* **67,** 627 – 630

Di Rago J P, Colson A-M (1988). Molecular basis for resistance to antimycin and diuron Q-cycle inhibitors acting at the Q-I site in the mitochondrial ubiquinol-cytochrome C reductase in *Saccharomyces cerevisiae. Journal of Biological Chemistry* **263,** 12564-12570

Di Rago J-P, Coppee J-Y, Colson A-M (1989). Molecular basis for resistance to myxothiazol mucidin strobilurin A and stigmatellin cytochrome B inhibitors acting at the center of the mitochondrial ubiquinol cytochrome C reductase in *Saccharomyces cereviaiae. Journal of Biological Chemistry* **264,** 14543-14548

Duineveld Th L J, Beijersbergen J C M (1975). On the resistance to benomyl of fungi isolated from bulbs and corms. *Acta Horticulturae (Wageningen)* **47,** 143-148

Dux H, Sierotzki H, Meier-Runge F, Gisi U (2005). Sensitivity of *Venturia inaequalis* populations to anilinopyrimidine, DMI and QoI fungicides. *In*: Modern Fungicides and Antifungal Compounds IV. Eds. H-W Dehne, U Gisi, K-H Kuck, P E Russell, H Lyr. BCPC, Alton, UK pp. 45-54

E

Eastburn D M, Butler E E (1986). The occurrence of benomyl resistant isolates of *Trichoderma harzianum* in Costa Rican soils. *Phytopathology* **76,** 1066 (abstract)

Eckert J W (1987). *Penicillium digitatum* biotypes with reduced sensitivity to imazalil. *Phytopathology* **77,** 1728

Elmer P A G, Gaunt R E (1994). The biological characteristics of dicarboximide resistant isolates of *Monilinia fructicola* from New Zealand stone fruit orchards. *Plant Pathology* **43,** 130 – 137.

Source: www.frac.info
January 2013

Ehrenhardt H, Eichhorn K W, Thate R (1973). Zur Frage der Resistenzbildung von *Botrytis cinerea* gegenuber systemischen Fungiziden. Nachrichtenblatt des Deutschen Pflanzenschutzdienstes (Braunschueig) **25,** 49 – 50

Elad Y (1992). Reduced sensitivity of *Botrytis cinerea* to two sterol, biosynthesis inhibiting inhibiting fungicides: fenetrazole and fenethanil. *Plant Pathology* **41,** 47 – 54

Elad Y, Yunis H, Katan T (1992). Multiple fungicide resistance to benzimidazoles dicarboximides and diethofencarb in field isolates of *Botrytis cinerea* in Israel. *Plant Pathology* **41,** 41-46

Elad Y, Shpialter L, Korolev N, Mamiev M, Rav David D, Dori I, Ganot L, Shmuel D, Matan E, Messika Y. (2008) Integrated chemical and cultural control for grey mould (*Botrytis cinerea*) management in Lisianthus. *In*: Modern Fungicides and Antifungal Compounds IV. Proceedings of the 15th International Reinhardsbrunn Symposium. Eds. Dehne H-W, Gisi U, Kuck K-h, Russell P E, Lyr H. (in press)

Elmer P A G, Braithwaite M, Saville D J (1992). Changes in triforine sensitivity in populations of *Monilinia fructicola* from Hawkes Bay orchards. *Proceedings of the 45th. New Zealand Plant Protection Conference* **45,** 138 – 140

Esuruoso O F, Wood R K S (1971). The resistance of spores of resistant strains of *Botrytis cinerea* to quintozene tecnazene and dicloran. *Annals of Applied Biology* **68,** 271-279

F

Falloon R E, Follas G B, Butler R C, Goulder D S (2000). Resistance in *Peronospora viciae* to phenylamide fungicides: reduced efficacy of seed treatments of pea (*Pisum sativum*) and assessment of alternatives. *Crop Protection* **19,** 313 – 325

Fancelli M I, Kimati H (1991). Occurrence of iprodione resistant strains of *Alternaria dauci. Summa Phytopathologica* **17,** 135-146

Farber R B K, Chin K M, Leadbitter N (2002). Sensitivity of *Venturia inaequalis* to trifloxystrobin. *Pest Management Science* **58,** 261-267

Faretra F, Pollastro S (1993). Isolation, characterisation and genetic analysis of laboratory mutants of *Botryotinia fuckeliana* resistant to the phenylpyrrole fungicide CGA-173506. *Mycological Research* **97,** 620-624

Felsenstein F, Semar M, Stammler G (2010). Sensitivity of wheat powdery mildew (*Blumeria graminis* f.sp *tritici*) towards metrafenone. *Gesunde Pflanzen* **62**, 29-33

Fernandez-Ortuno D, Perez-Garcia A, Lopez-Ruiz F, Romero D, de Vicente A, Tores J A (2006). Occurrence and distribution of resistance to QoI fungicides in populations of *Podosphaera fusca* in south central Spain. *European Journal of Plant Pathology* **115,** 215 – 222

Fernandez-Ortuno D, Tores J A, de Vincente A, Perez-Garcia A (2008). Field resistance to QoI fungicides in *Podosphaera fusca* is not supported by typical mutations in the mitochondrial cytochrome b gene. *Pest Management Science* **64**, 694-702

Ferrin D M, Kabashima J N (1991). *In-vitro* insensitivity to metalaxyl of isolates of *Phytophthora citricola* and *Phytophthora parasitica* from ornamental hosts in Southern California USA. *Plant Disease* **75,** 1041 – 1044

Figueras-Roca M, Cristani C, Vannacci G (1996). Sensitivity of Trichoderma isolates and selected resistant mutants to DMI fungicides. *Crop Protection* **15,** 615 – 620

Fletcher J T, Yarham D J (1976). The incidence of benomyl tolerance in *Verticillium fungicola, Mycogone perniciosa* and *Hyphomyces rosellus* in mushroom crops. *Annals of Applied Biology* **84,** 343 – 354

Source: www.frac.info
January 2013

Fletcher J S, Wolfe M S (1981) Insensitivity of *Erysiphe graminis* f. sp. *hordei* to triadimefon, triadimenol and other fungicides. *Proceedngs of the Brighton Crop Protection Conference, Pests & Diseases 633 – 640*

Foerster H, Connell J H, Adaskaveg J E (2009). QoI resistance in *Fusicladium carpophilum* populations from almond in California. *Phytopathology* **99** S35

Forster B, Staub T (1996). Basis for use strategies of anilinopyrimidine and phenylpyrrole fungicides against *Botrytis cinerea. Crop Protection* **15,** 529-537

Fourie P H, Holz G (2001). Incomplete cross-resistance to folpet and iprodione in *Botrytis cinerea* from grapevine in South Africa. *South African Journal of Enology and Viticulture* **22,** 3-7

Fraaije B A, Burnett F J, Clark W S, Motteram J, Lucas J A (2005). Resistance development to QoI inhibitors in populations of *Mycosphaerella graminicola* in the UK. In: *Modern Fungicides and Antifungal Compounds IV.* BCPC, Al;ton, UK pp. 63-72

Fraaije B A, Lucas J A (2003). QoI resistance development in populations of cereal pathogens in the UK. *Proceedings of the BCPC International Congress – Crop Science & Technology* 689 – 694

FRAC. Where a reference is given as 'FRAC' please refer to the FRAC website: www.frac.info and the appropriate Working Group page. When a date is given, this indicates the first report to the FRAC Working Group

FRAG UK. Indicates that a verified case was reported to the FRAG UK Committee

Freeman J, Ward E, Gutteridge R J, Bateman G L (2005). Methods for studying population structure, including sensitivity to the fungicide siltthiofam, of the cereal take-all fungus, *Gaeumannomyces graminis* var. *tritici. Plant Pathology* **54,** 686-698

Fujimura M, Kamakura T, Inoue K, Yamaguchi I (1994). Amino acid alterations in the beta-tubulin gene of *Neurospora crassa* that confer resistance to carbendazim and diethofencarb. *Current Genetics* **25,** 418-422

G

Gafur A, Tanaka C, Shimizu K, Ouchi S, Tsuda M (1998). Genetic analysis of *Cochliobolus heterostrophus* polyoxin resistant mutants. *Mycoscience* **39,** 155-159

Garibaldi A, Migheli Q, Gullino M L (1987). Evaluation of the efficacy of several fungicides against *Cryptoclina cyclaminis* on Cyclamen. *Meded. Fac. Landbouwwet. Rijksuniv. Gent* **52,** 859-865

Gasonshi K, Takanashi K (1973). Resistance of pear black spot pathogen to polyoxin. *Annals of the Phytopathological Society of Japan* **39,** 173-174

Geary B, Johnson D A, Hamm P B, James S, Rykbost K A (2007). Potato silver scurf affected by tuber seed treatments and locations, and occurrence of fungicide resistant isolates of *Helminthosporium solani.* Plant Disease **91** 315-320

Genet J L, Jaworska G (2009). Baseline sensitivity to proquinazid in *Blumeria graminis* f. Sp. *Tritici* and *Erysiphe necator* and cross resistance with other fungicides. *Pest Management Science* **65** 878-884

Georgopoulos S G, Dovas C (1973). A serious outbreak of strains of cercospora beticola resistant to benzimidazole fungicides in northern Greece. *Plant Disease Reporter* **62,** 205 – 208

Source: www.frac.info
January 2013

Giannopolitis C N (1978). Occurrence of strains of *Cercospora beticola* resistant to tri-phenyl tin fungicides in Greece. *Plant Disease Reporter* **62,** 205-208

Giannopolitis C N, Chrysayi-Tokousbalides M (1980). Biology of tri phenyl tin resistant strains of *Cercospora beticola* from sugar beet. *Plant Disease* **64,** 940 – 942

Gilmenez V I, Luisi N (1978). Tolerance to benomyl in *Phoma tracheiphila*. *Phytopathogogia Mediterranea* **17,** 77 (abstract)

Gisi U, Pavic L, Stanger C, Hugelshofer U, Sierotzki H (2005). Dynamics of *Mycosphaerella graminicola* populations in response to selection by different fungicides. . In: *Modern Fungicides and Antifungal Compounds IV.* BCPC, Al;ton, UK pp. 89-102

Gisi U, Sierotzki H, Cook A, McCaffery A (2002). Mechanisms influencing the evolution of resistance to Qo inhibitor fungicides. *Pest Management Science.* **58,** 859-867

Gisi U, Waldner M, Kraus N, Dubuis P H, Sierotzki H (2007). Inheritance of resistance to carboxylic acid amide fungicides in *Plasmopara viticola. Plant Pathology* **56** 199-208

Gossen B D, Anderson K L (2004). First report of resistance to strobilurin fungicides in *Didymella rabiei. Canadian Journal of PLant Pathology* **26,** 411

Goszczynski W, Cimanowski J, Bachnacki R (1988). First note on the occurrence of a strain of *Sphaerotheca mors-uvae* Schw. –Berk. with decreased ensitivity to triadimefon. *Fruit Science Reports (Skierniewice)* **15,** 181 – 184

Goto M, Hikota T, Nakajima M, Takikawa Y, Tsuyumi S (1994). Occurrence and properties of copper resistance in plant pathogenic bacteria. *Annals of the Phytopathological Society of Japan* **60,** 147-153

Griffee P J (1973). Resistance to benomyl and related fungicides in *Colletotrichum musae. Transactions of the British Mycological Society* **60,** 433 - 439

Griffin M J, Drummond M, Yarham D J, King J E, Brown M (1982). Benzimidazole resistance in *Pseudocercosporella herpotrichoides*, the cause of eyespot disease of cereals. *International Society for Plant Pathology, Chemical Control Newsletter* **1,** 7 – 8

Griffin M, Fisher N (1985). Laboratory studies on benzimidazole resistance in *Septoria tritici*. *uelletin OEPP* **15,** 505 – 512

Grindle M (1984). Isolation and characterisation of vinclozolin resistant mutants of *Neurospora crassa. Transactions of the British Mycological Society* **82,** 635-644

Gullino M L, Mescalchin E, Mezzalama M (1997). Sensitivity to cymoxanil in populations of *Plasmopara viticola* in northern Italy. *Plant Pathology* **46,** 729-736

Gullino M L, Gilardi G, Tinivella F, Garibaldi A (2004). Observations on the behaviour of different populations of *Plasmopara viticola* resistant to QoI fungicides in Italian vineyards. *Phytopathologia Mediterranea* **43,** 341-350

Gutierrez-Alonso J G, Gutierrez-Alonso O, Nieto-Angel D, Teliz-Ortiz D, Zavaleta-Mejia E, Delgadillo-Sanchez F, Vaquera-Huerta H (2003). Evaluation of resistance to imazalil, prochloraz, and azoxystrobin of *Colletotrichum gloeosporioides* (penz.) Penz. y Sacc. isolates and control of Mango (*Mangifera indica L.*) anthracnosis during postharvest. *Revista Mexicana de Fitopatologia* **21,** 379 - 382

H

Source: www.frac.info
January 2013

Hanson L E, Schwager S J, Loria R (1996). Sensitivity to thiabendazolwe in Fusarium species associated with dry rot in potatoes. *Phytopathology* **86,** 378-384

Harrison J G (1984). *Botrytis cinerea* as an important cause of chocolate spot in field beans. *Transactions of the British Mycological Society* **83,** 631-638

Hartill W F T, Tompkins G R, Kleinshaw P J (1983). Development in New Zealand of resistance to dicarboximide fungicides in *Botrytis cinerea* to acylalanines in *Phytophthora infestans* and to guazatine in *Penicillium italicum*. *New Zealand Journal of Agricultural Research* **26,** 261 – 270

Hasti A C, Georgopoulos S G (1971). Mutational resistance to fungitoxic benzimidazole derivatives in *Aspergillus nidulans. Journal of General Microbiology* **65,** 371-374

Heaney S P, Hall A A, Davies S A, Olaya G (2000). Resistance to fungicides in the QoI-STAR cross resistance group: current perspectives. *Proceedings of the BCPC Conference – Pests & Diseases* 755 - 762

Henry M J, Trivellas A E (1989). Laboratory induced fungicide resistance to benzimidazole and azole fungicides in *Cercospora beticola. Pesticide Biochemistry and Physiology* **35,** 89 – 96

Herbert J A, Grech N M (1985). A strain of *Guignardia citricarpa*, the citrus black spot pathogen, resistant to benomyl in South Africa. *Plant Disease* **69,** 1007 (abstract)

HGCA (2005). Wheat Disease Management Guide – 2005 Update. Home Grown Cereals Authority, London UK

Hill S N, Hausbeck M K (2008). Virulence and fungicide sensitivity of *Phytophthora cactorum* isolated from American ginseng gardens in Wisconsin and Michigan. *Plant Disease* **92**, 1183-1189

Hippe S, Koller W (1986). Ultrastructure and sterol composition of laboratory strains of *Ustilago avenae* resistant to triazole fungicides. *Pesticide Biochemistry and Physiology* **26,** 209-219

Hollomon D W (1978). Competitive ability and ethirimol sensitivity in strains of barley powdery mildew. *Annals of Applied Biology* **90,** 195-204

Hollomon D W, Wheeler I, Dixon K, Longhurst C, Skylakakis G (1997). Defining the resistance risk of the new powdery mildew fungicide quinoxyfen. *Pesticide Science* **51,** 347-351

Holz B (1979). Űber eine resistenzersheinung von *Botrytis cinerea* an Reben gegen die neuen Kontaktbotrytizide im Gebeit der Mittelmosel. *Weinberg und Keller* **26,** 18 – 25

Hori M, Kakiki K, Misato T (1976). Mechanism of polyoxin resistance in *Alternaria kikuchiana. Journal of Pesticide Science* **1,** 31-40

Hosokawa H., Yamanaka H., Haramoto M, Sano S, Yokota C, Hamamura H. (2006), Occurrence and biological properties of cyflufenamid-resistant *Sphaerotheca cucurbitae*. *Japanese. Journal of Phytopathol*ogy **72**: 260-261 (Japanese abstr.).

Hsiang T, Chastagner G A (1990). Parasitic fitness of benzimidazole and dicarboximide resistant isolates of *Botrytis cinerea Botrytis elliptica* and *Botrytis tulipae.Phytopathology* **80,** 978

Hu J H, Hong C X, Stomberg E L, Moorman G W (2008). Mefenoxam sensitivity and fitness analysis of *Phytophthora nicotianae* isolates from nurseries in Virginia USA. *Plant Pathology* **57**, 728-736

Source: www.frac.info
January 2013

Hubbard J C, Subbarao, Koike S T (1997). Development and significance of dicarboximide resistance in *Sclerotinia minor* isolates from commercial lettuce fields in California. *Plant Disease* **81,** 148-153

Hunter T, Jordan V W, Kendall S J (1986). Fungicide sensitivity changes in *Rhynchosporium secalis* in glasshouse experiments. *Proceedings of the British Crop Protection Conference, Pests & Diseases* 523 – 536

Hutton D G (1988). The appearance of dicarboximide resistance in *Alternaria alternata* in passionfruit in South-East Queensland Australia. *Australasian Plant Pathology* **17,** 34-36

Hwang B K, Yun J H (1986). Variability in sensitivity to polyoxin B of isolates of *Alternaria mali* and decreased fitness of polyoxin resistant isolates. *Journal of Phytopathology* **115,** 305-312

I

Ieki H (1994). Emergence of benzimidazole resistant strains of *Elsinoe fawcetti* Jenkins in citrus orchards in Japan. *Annals of the Phytopathological Society of Japan* **60,** 501 – 506

Iida W (1975). On the tolerance of plant pathogenic fungi and bacteria to fungicides in Japan. *Japanese Pesticide Information* **23,** 13-16

Ilott T W, Ingram D S, Rawlinson C J (1987). Studies of fungicide resistance in *Pyrenopeziza brassicae* cause of light leaf spot disease of oilseed rape and other brassicas. *Transactions of the British Mycological Society* **88,** 515-523

Ishii H (2004). Fungicide resistance: a factor limiting integrated disease control. *Proceedings of the 15th. International Plant Protection Congress* Ed. Guo Yu-yuan. p. 216

Ishii H, Yamaguchi A (1981). Resistance of *Venturia nashicola* to thiophanate-methyl and bonomyl existence of weakly resistant isolates and its practical significance. *Annals of the Phytopathological Society of Japan* **4,** 528 – 533

Ishii H, Fraaije B A, Sugiyama T, Noguchi K, Nishimura K, Takeda T, Amano T, Hollomon D W (2001). Occurrence and molecular characteristics of strobilurin resistance in cucumber powdery mildew and downy mildew. *Phytopathology* **91,** 1166-1171

Ishii H, Noguchi K, Tomita Y, Umemoto S, Nishimura K (1999). Occurrence of strobilurin resistance in powdery mildew and downy mildew on cucumbers. . *Annals of the Phytopathological Society of Japan* **65,** 655

Ishii, H., Fountaine J., Miyamoto, T., Nishimura, K. and Tomita, Y. (2007), Occurrence of a mutation in the succinate dehydrogenase gene found in some isolates of cucumber *Corynespora* leaf spot fungus resistant to boscalid. *Japanese Journal of Phytopatho*logy **74**: in press (Japanese abstr.).

Ishii H (2008). Fungicide research in Japan, an overview. *In*: Modern Fungicides and Antifungal Compounds IV. Proceedings of the 15th International Reinhardsbrunn Symposium. Eds. Dehne H-W, Gisi U, Kuck K-h, Russell P E, Lyr H. (in press)

Ito I, Yamaguchi T (1977). Occurrence of kasugamycin resistant rice blast fungus influenced by the application of fungicides. *Annals of the Phytopathological Society of Japan***43,** 301-303

Ito Y, Maraguchi H, Seshime Y, Oita S, Yanagi S O (2004). Flutolanil and carboxin resistance in *Coprinus cinereus* conferred by a mutation in the cytochrome b560 subunit of succinate dehydrogenase complex (Complex II). *Molecular Genetics and Genomics* **272,** 328 – 335

Source: www.frac.info
January 2013

J

Jarvis W R, Hargreaves A J (1973). Tolerance to benomyl in *Botrytis cinerea* and *Penicillium corymbiferum. Plant Pathology* **22,** 139-141

Jarvis W R, Slingsby K (1975). Tolerance of *Botrytis cinerea* and rose powdery mildew to benomyl. *Canadian Plant Disease Survey* **55,** 44

Jones A L, Ehret G R (1976). Isolation and characterisation of benomyl tolerant strains of *Monilinia fructicola. Plant Disease Reporter* **60,** 765 – 769

Jones A L, Ehret G R (1981). Resistance of *Coccomyces hiemalis* to benzimidazole fungicides. *Plant Disease* **64,** 767 – 769

Jones W B, Thompson S V (1982). The effects of fungicide treatments on yield and quality of tomato plants infected with *Leveillula taurica. Phytopathology* **72,** 970 (abstract)

Joseph M C, Coffey M D (1984). Development of laboratory resistance to metalaxyl in *Phytophthora citricola. Phytopathology* **74,** 1411 – 1414

Joseph-Horne T, Hollomon D W, Heppner C (2000). Silthiofam interferes with mitochondrial function in 'take-all' disease of wheat. *Proceedings of the Brighton Crop Protection Conference – Pests & Diseases* 883-888

Joya C (1982). Identification of sigatoka pathogens and monitoring for benzimidazole resistance. *Phytopathology* **72,** 453

K

Kalamarakis A E, De Waard M A, Ziogas B N, Georgopoulos S G (1991). Resistance to fenarimol in *Nectria haematococca* var *cucurbitae. Pesticide Biochemistry and Physiology* **40,** 212 – 220

Kanetis L, Forster H, Jones C A, Borkovich K A, Adaskaveg J E (2008). Characterization of genetic and biochemical mechanisms of fudioxonil and pyrimethanil resistance in field isolates of *Penicillium digitatum.Phytopathology* **98** 205-214.

Kappas A, Georgopoulos S G (1968). Radiation induced resistance to dodine fungicide in *Hypomyces. Experietia (Basel)* **24,** 181 – 182

Karaoglanidis G S, Ionnidis P M, Thanossoulopoulos CC (2000). Reduced sensitivity of *Cercospora beticola* isolates to sterol demethylation inhibiting fungicides. *Plant Pathology* **49,** 567 – 572

Katan T, Shabi E (1981). REsistance to dicarboximide fungicides in laboratory isolates of *Monilinia laxa. Phytoparasitica* **9,** 231-232

Katan T, Dunn M T, Papavizas G C (1984). Genetics of fungal resistance in *Talaromyces flavus*. *Canadian Journal of Microbiology* **30,** 1079-1087

Katan T, Elad Y, Yunis H (1989). Resistance to diethofencarb NPC in benomyl resistant field isolates of *Botrytis cinerea. Plant Pathology* **38,** 86-92

Kato T, Suzuki K, Takahashi J, Kamoshita K (1984). Negatively correlated cross resistance between benzimidazole fungicides and methyl N-(3, 5-dichlorophenyl) carbamate. *Journal of Pesticide Science* **9,** 489-495

Kendall S J, Hollomon D W (1990). DMI resistance and sterol 14-alpha demethylation in *Rhychosporium secalis. Proceedings of the British Crop Protection Conference Pests & Diseases* 1129-1134

Kendall S J, Hollomon D W, Cooke L R, Jones D R (1993). Changes in sensitivity to DMI fungicides in *Rhynchosporium secalis. Crop Protection* **12,** 357 – 362

Source: www.frac.info
January 2013

Keon J P R, White G A, Hargreaves J A (1991). Isolation, characterization and sequence of a gene conferring resistance to the systemic fungicide carboxin from the maize smut pathogen, *Ustilago maydis. Current Genetics* **19**, 475-481

Khilare V C, Deokate A S, Ganawane L V (2003). Occurrence of aluminium phosethyle (allitte) resistance in *Plasmopara viticola* causing downy mildew of grapevine in Maharashtra. *Journal of Phytological Research* **16,** 239 – 241

Kiebacher H, Hoffmann G M (1976). Benzimidazole resistance in *Venturia inaequalis. Zeitschrift fuer Pflanzenkrankheiten und Pflanzenschutz* **83,** 352 – 358

Kim Y-S, Dixon E W, Vincelli P, Farman M L (2003). Field resistance to strobilurin (QoI) fungicides in *Pyricularia grisea* caused by mutations in the mitochondrial cytochrome b gene. *Phytopathology* **93,** 891-900

Kleitman F, Shtienberg D, Blachinsky D, Oppenheim D, Zilberstaine M, Dror O, Manulis S (2005). *Erwinia amylovora* populations resistant to oxolinic acid in Israel: prevalence, persistence and fitness. *Plant Pathology* **54,** 108-115

Köller W, Smith F D, Reynolds K L (1991). Phenotypic instability of flusilazole sensitivity in *Venturia inaequalis*. *Plant Pathology* **40,** 608 – 611

Kousik C S, Keinath A P (2008). First report of insensitivity to cyazofamid among isolates of *Phytophthora capsici* from the southeastern United States. *Plant Disease* **92**, 979

L

Lacy G H, Stromberg V K, Cannon N P (1984). *Erwinia amylovora* mutants and *in planta* derived trans conjugants resistant to oxytetracycline. *Canadian Journal of Plant Pathology* **6,** 33-39

Lambert D H, Wuest P J (1973). Tolerance of *Verticillium malthousii* isolates to benomyl in relation to linear growth, gepgraphical origin, spray volume or zineb tolerance. ***Phytopathology*** **63,** 203 (abstract).

Lambert D H, Salas B (1994). Metalaxyl insensitivity of *Phytophthora erythroseptica* isolates causing pink rot of potato in Maine. *Plant Disease* **78,** 1010

Lamboy J S, Paxton J D (1992). Metalaxyl sensitivity selection within *Phytophthora megasperma* fsp. *glycinea. Plant Disease* **76,** 932 – 936

Langston D (2002). Quadris resistance in Gummy Stem Blight confirmed. *Georgia Extension Vegetable News.* **2,** 1

Lasseron-De Falandre A, Debieu D, Bach J, Malosse C, Leroux P (1999). Mechanisms of resistance to fenpropimorph and terbinafine, two sterol biosynthesis inhibitors, in *Nectria haematococca*, a phytopathogenic fungus. *Pesticide Biochemistry and Physiology* **64,** 167-184

Lei Chen, Shusheng Zhu, Xiaohong Lu, Zhili Pang, Meng Cai, Xili Liu (2012). Assessing the risk that *Phytophthora melonis* can develop a point mutation (V1109L) in CesA3 conferring resistance to carboxylic acid amide fungicides. *Plos One* **7** (7), e42069

Leroux P, Lafon R, Gredt M (1982). Resistance of Botrytis cinerea to benzimidazole and dicarboximide fungicides situation in Alsace Bordeaux and Champagne vineyards France. *Bulletin OEPP* **12,** 137 - 144

Leroux P, Clerjeau M (1985). Resistance of *Botrytis cinerea* and *Plasmopara viticola* to fungicides in French vineyards. *Crop Protection* **4,** 137 – 160

Source: www.frac.info
January 2013

Leroux P, Berthier G (1988). Resistance to carboxin and fenfuram in *Ustilago nuda* Jens. Rostr. the causal agent of barley loose smut. *Crop Protection* **7,** 16-19
Leroux P, Marchegay P (1991). Caractérisation des souches de *Pseudocercosporella herpotrichoides* agent du Piétin-verse des céréales, resistantes au prochloraze, isolées en France sur blé tendre d'hiver. *Agrononie* **11,** 767 – 776
Li H X, Xiao C L (2008). Characterization of fludioxonil resistant and pyrimethanil resistant phenotypes of *Penicillium expansum* from apple. *Phytopathology* **98**, 427-435
Li H, Leifert C (1994). Development of resistance in *Botryotinia fuckeliana* (de Barry) Whetzel against the biological control agent *Bacillus subtilis* CL27. *Zeitschrift fur Pflanzenkrankheiten und Pflanzenschutz* **101**, 414-8.
Littrell R H (1974). Tolerance in *Cercospora arachidicola* to benomyl and related fungicides. *Phytopathology* **64,** 1377 - 1378
Littrell R H (1977) Population dynamics and control of benomyl tolerant and sensitive pecan scab strains. *Proceedings of the American Phytopathological Society* **3,** 1976
Liu X, Yin Y N, Wu J B, Jiang J H, Ma Z H (2010). Identification and Characterization of Carbendazim-Resistant Isolates of *Gibberella zeae* *Plant Disease* **94**, 1137-1142
Locke T, Thorpe I G (1976). Benomyl tolerance in *Verticillium dahliae* Kleb. *Plant Pathology* **25,** 59
Locke T, Scrace J, Peace J M (1997). Resistance of *Phytophthora porri* to metalaxyl. *Pesticide Science* **51,** 371 – 374
Lu Y L, Sutton T B, Ypema H (2003). Sensitivity of *Alternaria mali* from north Carolina apple orchards to pyraclostrobin and boscalid. *Phytopathology* **93,** S54 (Abstract)
Lu X H, Zhu S S, Bi Y, Liu X L, Hao J J (2010). Baseline sensitivity and resistance risk assessment of *Phytophthora capsici* to iprovalicarb. *Phytopathology*, **100,** 1162-1168
Lucas J A, Bower L A, Coffey M D (1990). Fungicide resistance in soil-borne *Phytophthora* species. *EPPO Bulletin* **20,** 199-206

M
Ma B, Uddin W (2009). Fitness and competitive ability of an azoxystrobin resistant G143A mutant of *Magnaporthe oryzae* from perennial ryegrass. *Plant Disease* **93** 1044-1049
Ma, Z, Michailides T J (2004). Characterization of iprodione-resistant Alternaria isolates from pistachio in California. *Pesticide Biochemistry and Physiology* **80,** 75 – 84
Ma Z, Felts D, Michailides T J (2003). Resistance to azoxystrobin in Alternaria isolates from pistachio in California. *Pesticide Biochemistry and Physiology* **77,** 66 - 74
Ma Z, Luo Y, Michailides T J (2001). Resistance of *Botryosphaeria dothidea* from pistachio to iprodione. *Plant Disease* **85,** 183-188
Magie R O, Wilfret G J (1974). Tolerance of *Fusarium oxysporum* f sp. *gladioli* to benzimidazole fungicides. *Plant Disease Reporter* **58,** 256 – 259
Malathrakis N E (1989). Resistance of *Botrytis cinerea* to dichlofluanid in greenhouse vegetables. *Plant Disease* **73,** 138-141

Source: www.frac.info
January 2013

Malathrakis N E, Vakalounakis D J (1983). Resistance to benzimidazole fungicides in the gummy stem blight pathogen *Didymella bryoniae* on cucurbits. *Plant Pathology* **32,** 395 – 400
Manulis S, Kleitman F, Shtienberg D, Shwartz H, Oppenheim D, Zilberstaine M, Shabi E (2003). Changes in the sensitivity of *Erwinia amylovora* populations to streptomycin and oxolinic acid in Israel. *Plant Disease* **87,** 650-654
Maria R, Sullia S B (1986). Acquired resistance of *Alternaria solani* and *Sclerotium rolfsii* to polyoxin D. *Journal of Phytopathology* **116,** 60-66
Markoglou A N, Ziogas B N (1999). Genetic control of resistance to fenpropimorph in *Ustilago maydis. Plant Pathology* **48,** 521-530
Markoglou A N, Ziogas B N (2000). Genetic control of resistance to tridemorph in *Ustilago maydis. Phytoparasitica* **28,** 349-360
Markoglou A N, Ziogas B N (2001). Genetic control of resistance tothe piperidine fungicide fenpropidin in *Ustilago maydis. Journal of Phytopathology* **149,** 551-559
Markoglou A N, Malandrakis A A, Vitoratos A G, Ziogas B N (2006). Characterization of laboratory mutants of *Botrytis cinerea* to QoI fungicides. *European Journal of Plant Pathology* **115,** 149 – 162
Markoglou A N, Doukas E G, Ziogas B N (2008). Phenylpyrrole resistance and aflatoxin production in *Aspergillus parasiticus* Speare. *International Journal of Food Microbiology* **127** 268-275
Martin S B, Lucas L T, Campbell CL (1984). Comparative sensitivity of *Rhizoctonia solani* and Rhizoctonia like fungi to selected fungicides in-vitro. *Phytopathology* **74,** 778 – 781
Matsuzaki M, Azegami K, Chata K-I (1981). Streptomycin resistance in pathogenic bacteria isolated from diseased lettuce. *Annals of the Phytopathological Society of Japan* **47,** 297-300
Mavroedi V I, Shaw M W (2005). Sensitivity distributions and cross resistance patterns of *Mycosphaerella graminicola* to fluquinconazole, prochloraz and azoxystrobin over a period of 9 years. *Crop Protection* **24,** 259-266
McKay G J, Egan D, Morris E, Brown A E (1998). Identification of benzimidazole resistance in *Cladobotryum dendroides* using a PCR-based method. *Mycological Research* **102,** 671 – 676
McGrath M T, Shishkoff N (2003a). Resistance to strobilurin fungicides in *Podosphaera xanthii* associated with reduced control of cucurbit powdery mildew in a research field. *Phytopathology* **93,** S59
McGrath M T, Shishkoff N (2003b). First report of the cucurbit powdery mildew fungus (*Podosphaera xanthii)* resistant to strobilurin fungicides in the United States. *Plant Disease* **87,** 1007
McHugh J B, SchreiberJ R (1984). Tolerance of *Verticillium dahliae* to benzimidazoles. *Plant Disease* **68,** 424 – 427
Meissner S, Stammler G. (2010). *Monilinia laxa, M. fructigena and M. fructicola:* Risk estimation of resistance to QoI fungicides and identification of species with cytochrome b gene sequences. *Journal of Plant Diseases and Protection.* **117**, 162-167
Metcalfe R J, Shaw M W, Russell P E (2000). The effect of dose and mobility on the strength of selection for DMI fungicide resistance in inoculated field experiments. *Plant Pathology* **49,** 546-557
Meyer E (1976). Resistance development against systemic fungicides benzimidazole derivatives in *Colletorichum lindemuthianum. Mitteilungen aus der Biologischen Bundesanstalt fur Land- und Forstwirtschaft* **(166),** 7 – 135

Source: www.frac.info
January 2013

Miao V, Higgins V J (1986). Detection of induced susceptibility in tomato using mutants of *Cladosporium fulvum* tolerant to cycloheximide or benomyl. *Canadian Journal of Botany* **64,** 1299-1305
Miller T C, Gubler W D (2003). *Uncinula necator* retains high resistance levels to triadimefon in a survey of California populations despite product absence for fourteen years. *Phytopathology* **93,** S113
Minsavage G V, Cantero B I, Stall R E (1990). Plasmid mediated resistance to streptomycin in *Xanthomonas campestris* pv. *vesicatoria. Phytopathology* **80,** 719-723
Miyamoto T., Ishii H., Seko T., Tomita Y., Kobori S. Ogawara T. (2007). Occurrence of boscalid-resistant isolates of cucumber Corynespora leaf spot fungus (*C. cassiicola*). *Japanese Journal of Phytopathol*ogy **74**: in press (Japanese abstr.).
Miyamoto T, Ishii H, Seko T, Kobori S, Tomita Y. (2009). Occurrence of *Corynespora cassiicola* isolates resistant to boscalid on cucumber in Ibaraki prefecture, Japan. *Plant Pathology* **58,** 1144-1151
Miyamoto T, Ishii H,Tomita Y (2010a). Occurrence of boscalid resistance in cucumber powdery mildew in Japan and molecular characterization of the iron-sulfur protein of succinate dehydrogenase of the causal fungus. *Journal of General Plant Pathology* **76**, 261-267
Miyamoto T, Ishii H, Stammler G, Koch A, Ogawara T, Tomita Y, Fountaine J M, Ushio S, Seko T, Kobori S. (2010b). Distribution and molecular characterisation of *Corynespora cassiicola* isolates resistant to boscalid. *Plant Pathology* **59,** 873-881
Molinero V, Leroux P, Tivoli B, Champion R, Said J (1993). Resistance to benzimidazole fungicides in pathogens of Ascochta diseases of peas. *Seed Science and Technology* **21,** 531 – 535
Moller W J, Beutel J A, Reil W O, Zoller B G (1972). Fire blight resistance to streptomycin in California. *Phytopathology* **62,** 779
Mondal S N, da Silva A G, Dewdney M M (2009). Resistance to strobilurin fungicides in a population of *Alternaria alternata* causing Alternaria brown spot of citrus. APS Meeting, S88
Moorman G W, Arora N, Kim S H (2002). Propamocarb resistance in species of *Pythium. Phytopathology* **92,** S58 (meeting abstract)
Moorman G W, Kang S, Geiser D M, Kim S H (2002). Identification and characterisation of *Pythium* species associated with greenhouse floral crops in Pennsylvania. *Plant Disease* **86,** 1227 – 1231
Moorman G W, Kim S H (2004). Species of *Pythium* from greenhouses in Pennsylvania exhibit resistance to propamocarb and mefenoxam. *Plant Disease* **88,** 630-632
Muirhead T F (1974). Resistance to benzimidazole fungicides in blue mold of citrus in Queensland. *Australian Journal of Experimental Agriculture and Animal Husbandry* **14,** 698 – 701
Munro J M, Dolan A, Williamson B (1988). Cane spot (*Elsinoe veneta*) in red raspberry: infection periods and fungicidal control. *Plant Pathology* **37,** 390-396

N

Nachmias A, Barash I (1976). Decreased permeability as a mechanism of resistance to methylbenzimidazol-2-yl carbamate in *Sporobolomyces roseus. Journal of General Microbiology* **94,** 167 – 172

Source: www.frac.info
January 2013

Naegler M, Diaconu V, Alexandria A A (1977). The resistance of powdery mildew vine *Uncinula necator*and powdery mildew cucumbers *Sphaerotheca fuliginea* to benzimidazole systemic fungicides. *Analele Institutului de Cercetari Pentru Protectia Plantelor* **12,** 345 – 352

Napier B A S, Bayles R A, Stigwood P L (2000). Sensitivity of powdery mildew and yellow rust to DMI, morpholine and strobilurin fungicides in England and Scotland. *Proceedings of the BCPC Conference Pests & Diseases, 427-434*

Noble M, Maggarvie Q D, Hams A F, Leaf L L (1966). Resistance to mercury of *Pyrenophora avenae* in Scottish seed oats. *Plant Pathology* **15,** 23-28

Nomura H, Paik S-Y, Izuhara M, Sugiyama M (1991). Resistant mechanisms to blasticidin S in *Streptomyces lividans*. *Korean Biochemical Journal* **24,** 327-330

Nuninger-Ney C, Schwinn F J, Staub T (1989). *In vitro* selection of sterol biosynthesis inhibitor (SBI) resistant mutants in *Monilinia fructicola* (Wint.) Honey. *Netherlands Journal of Plant Pathology* **95,** 137 – 150

O

O'Brien R G, Vawdrey L L, Glass R J (1988). Fungicide resistance in cucurbit powdery mildew *Sphaerotheca fuliginea* and its effect on field control. *Australian Jounal of Experimental Agriculture* **28,** 417-424

Ogawa K (1988). Damage by Bakanae disease and its chemical control. *Japanese Pesticide Information* **52,** 13-15

Ogawa J M, Manji B T, Bose E A (1981). Detection of benomyl resistant *Monilinia laxa* on apricots. *Phytopathology* **71,** 893

Olaya G, Cleere S, Stanger C, Burbidge J, Hall A, Windass J (2003). A novel potential target site QoI fungicide resistance mechanism in *Pythium aphanidermatum. Phytopathology* **93,** S67

Olaya G, Holm A (2001). Sensitivity of *Didymella bryoniae* isolates to azoxystrobin. *Phytopathology* **91,** S67-S68

Omatsu N, Tomihama T, Nonaka Y (2012). Incidence of strobilurin and benzimidazole resistant strains of *Pestalotiopsis longiseta*, causal agent of gray blight, and practical control in tea field of Kagoshima Prefecture. *Japanese Journal of Phytopathology*, **78,** 3-9

Orth A B, Sfarra A, Pell E J, Tien M (1994). Characterization and genetic analysis of laboratory mutants of *Ustilago maydis* resistant to dicarboximide and aromatic hydrocarbon fungicides. *Phytopathology* **84,** 1210-1214

P

Pasche J S & Gudmestad N C (2008). Prevalence, competitive fitness and impact of the F129L mutation in *Alternaria solani* from the United States. *Crop Protection* **27**, 427-435

Pasche J S, Piche L M, Gudmestad N C (2005). Effect of the F129L mutation in *Alternaria solani* on fungicides affecting mitochondrial respiration. *Plant Disease* **89,** 269-278

Pasche J S, Wharam C M, Gudmestad N C (2004). Shift in sensitivity of *Alternaria solani* to QoI fungicides. *Plant Disease* **88,** 181 – 187

Pasche J S, Wharam C M, Gudmestad N C (2002). Shift in sensitivity of *Alternaria solani* (potato early blight) to strobilurin fungicides. *Proceedings of the BCPC Conference Pests & Diseases* 841-846

Paulus A O, Nelson J, Besemer S (1976). Resistance of *Septoria leucanthemi* to benzimidazole fungicides. *Plant Disease Reporter* **60,** 695 - 697

Source: www.frac.info
January 2013

Pearson R C (1980). Occurrence of benomyl resistant strains of *Uncinula necator* on grapes in New York USA. *Phytopathology* **70,** 467
Pearson R C, Taschenberg E F (1980). Benomyl resistant strains of *Uncinula necator* on grapes. *Plant Disease* **64,** 677 – 680
Pennucci A, Beever R E, Laracy E P (1990). Dicarboximide resistant strains of *Microdochium nivale* in New Zealand. *Australasian Plant Pathology* **19,** 38-41
Penrose L J, Koffmann W, Nicholls M R (1985). Field occurrence of vinclozolin resistance in *Monilinia fructicola. Plant Pathology* **34,** 228-234
Peters R D, Platt H W, Drake K A, Coffin R H, Moorehead S, Clark M M, Al-Mughrabi K I, Howard R J (2008). First report of fludioxonil resistant isolates of Fusarium spp. causing potato seed-piece decay. *Plant Disease* **92**, 172
Plumbley R A, Hemandez M A, Thompson A K (1984). Benomyl tolerance in a strain of *Penicillium sclerotigenum* infecting yams and the use of imazalil as a means of control. *Tropical Agriculture* **61,** 182-185
Porter L D, Miller J S, Hamm P B, David N L, Gieck S L, Miller J S, Gunderson B, Inglis D A. (2009) Metalaxyl-M resistant Pythium species in potato production areas of the Pacific Northwest of the USA. *American Journal of Potato Research* **86** 315-326
Presly A H, Maude R B (1982). Tolerance in *Botrytis squamosa* to iprodione. *Annals of Applied Biology* **100,** 117-127
Prest G de, Poppe J (1988). Efficacy of fungicides against *Cylindrocladium scoparium* and their influence on Azalea cuttings. *Meded. Fac. Landbouwwet. Rijksuniv. Gent* **53,** 643-650
Proffer T J, Berardi R, Ma Z, Nugent J E, Ehret G R, McManus P S, Jones A L, Sundin G W (2006). Occurrence, distribution, and polymerase chain reaction-based detection of resistance to sterol demethylation inhibitor fungicides in populations of *Blumeriella jaapii* in Michigan. *Phytopathology* **96,** 709 – 717

QR

Reddy K P, Anilkumar T B (1989). Resistance development to mancozeb in *Helminthosporium halodes. Mysore Journal of Agricultural Sciences* **23,** 184-188
Redi H, Steinkellner S (1996). Proof of sensitivity reduction with oidium towards DMI fungicides in Austrian viticulture. *Mitteilungen Klosterneuburg* **46,** 181-188
Reimann S, Deising H B (2005). Inhibition of efflux mediated fungicide resistance in *Pyrenophora tritici-repentis* by a derivative of 4 '-hydroxyflavone and enhancement of fungicide activity. *Applied and Environmental Microbiology* **71,** 3269-3275
Remiro D, Kimati H (1974). Resistencia a benomil e tiofanato em *Mycosphaerella fragariae* (Tul.) Lind. *Biologico* **40,** 22-24
Reuveni M (2001). Improved control of powdery mildew (*Sphaerotheca pannosa*) of nectarines in Israel using strobilurin and polyoxin B fungicides; mixtures with sulfur; and early bloom applications. *Crop Protection* **20,** 663-668
Reuveni M, Eyal H, Cohen Y (1980). Development of resistance to metalaxyl in *Pseudoperonospora cubensis*. *Plant Disease* **64,** 1108 – 1109
Reynolds K L, Brenneman T B, Bertrand P F (1997). Sensitivity of *Cladosporium caryigenum* to propiconazole and fenbuconazole. *Plant Disease* **81,** 163 – 166
Richardson L T (1973). Adaptive tolerance of *Fusarium solani* to benzimidazole derivatives *in vitro. Canadian Journal of Botany* **51,** 1725-1732

Source: www.frac.info
January 2013

Rodriguez R, Melendez P L (1984). Chemical control of cowpea powdery mildew and foliar spots. *Journal of the Agricultural University P. R.* **68,** 445-455

Romano M L, Edgington L V (1985). Resistance to metalaxyl in *Phytophthora* crown rot and root rot of African violet. *Canadian Journal of Plant Pathology* **7,** 448 – 449

Russell P E, Gaujard C, Creange P, Daniels A (2001). Aspects of take-all control by fluquinconazole. *In:* Modern Fungicides and Antifungal Compounds III. Eds. H-W Dehne, U Gisi, K-H Kuck, P E Russell, H Lyr. AgroConcept GmbH, Bonn. pp. 91-102

S

Saito S, Cadie-Davidson L, Wilcox W F (2011). Practical resistance to fenhexamid *Botrytis cinerea* isolates from grapevines in New York. *Phytopathology*, **101,** S158

Sakurai H, Naito H (1976). A cross resistance of *Pyricularia oryzae* to kasugamycin and blasticidin S. *Journal of Antibiotics (Tokyo)* **29,** 1341-1342

Sakurai H, Kwano M, Goh N, Yaoita T, Aoyaki K, Naito H (1977). Sensitivity distribution of physiologic races of *Pyricularia oryzae* to kasugamycin. *Journal of Antibiotics (Tokyo)* **30,** 607-609

Samuels G J, Johnston P R (1980) Benomyl and the Verticillium diseases of cultivated mushrooms. *New Zealand Journal of Agricultural Research* **23,** 155 - 157

Sanders P L, Soika M D (1988). Metalaxyl resistance frequency in overwintering populations of *Pythium aphanidermatum* from metalaxyl control failure sites. *Phytopathology* **78,** 1510

Sanders P L, Coffey M D, Greer G D, Soika M D (1990). Laboratory induced resistance to fosetyl aluminium in a metalaxyl resistant field isolate of *Pythium apahanidermatum. Plant Disease* **74,** 690-692

Saniewska A (1985). Red staining of Narcissi leaves. *Ochr. Rosl.* **29,** 19-20

Sawada H, Sugihara M, Takagaki M, Nagayama K (2004). *Pest Management Science* **60,** 777-785

Schabi E, Ben-Yephet Y (1976). Tolerance of *Venturia pirina* to benzimidazole fungicides. *Plant Disease Reporter* **60,** 451 – 454

Schepers H T A M (1983). Decreased sensitivity of *Sphaerotheca fuliginea* to fungicides which inhibit ergosterol biosynthesis. *Netherlands Journal of Plant Pathology* **89,** 185 – 187

Schepers H T A M (1984). Persistence of resistance to fungicides in *Sphaerotheca fuliginea. Netherlands Journal of PLant Pathology* **90,** 165-171

Schepers H T A M (1985a). Development and persistence of resistance to fungicides in *Sphaerotheca fuligenea* in cucumbers in the Netherlands. *Doktorthesis Proefschrift van de Landbouwhogeschool te Wageningen*

Schepers H T A M (1985b). Changes during a three year period in the sensitivity to ergosterol biosynthesis inhibitors of *Sphaerotheca fuliginea* in the Netherlands. *Netherlands Journal of Plant Pathology* **91,** 105 - 118

Schroedder W T, Providenti R (1969). Resistance to benomyl in powdery mildew in cucurbits. Plant Disease Reporter **53**, 271 – 275

Schroth M N, Thomson S V, Moller W J (1979). Streptomycin resistance in *Erwinia amylovora. Phytopathology* **69,** 565-568

Source: www.frac.info
January 2013

Semar M, strobel D, Koch A, Klappach K, Stammler G. (2007). Field efficacy of pyraclostrobin against populations of *Pyrenophora teres* containing the F129L mutation in the cytochrome b gene. *Journal of Plant Diseases and Protection* **114** 117-119

Seppanen E (1983). Different tolerances of 14 Fusarium spp. to thiophanate-methyl. *Annales Agriculturae Fenniae* **22,** 120-121

Sergeva V, Nair N G, Verdana J R, Shen C, Barchia I, Spooner-Hart R (2002). First report of anilinopyrimidine resistant phenotypes in *Botrytis cinerea* on grapevines in Australia. *Australasian Plant Pathology* **31,** 299-300

Serrhini N, Maraite M, Meyer J A (1985). *In-vitro* selection of strains of *Phytophthora citrophthora* resistant to metalaxyl. *Bulletin OEPP* **15,** 443 - 450

Sheridan J E, Grbavac N, Sheridan M H (1985). Triadimenol insensitivity in *Pyrenophora teres. Transactions of the British Mycological Society* **85,** 338 – 341

Shim J-Y, Choi H-T, Yoon K-S (1994). Cell biological changes of validamycin resistant strain in *Coprinus cinereus. Korean Journal of Mycology* **22**, 31-35

Shew H D (1985). Response of *Phytophthora parasitica var nicotianae* to metalaxyl exposure. *Plant Disease* **69,** 559 – 562

Shim M-Y, Starr J L, Neller K P, Woodard K E, Lee TA Jr. (1998). Distribution of isolates of *Sclerotium rolfsii* tolerant to pentachloronitrobenzene in Texas peanut fields. *Plant Disease* **82,** 103-106

Sierotzki H, Kraus N, Assemat P, Stanger C, Cleere S, Windass J, Gisi U (2005). Evolution of resistance to QoI fungicides in *Plasmopara viticola* populations in Europe. *In*: Modern Fungicides and Antifungal Compounds IV. Eds. H-W Dehne, U Gisi, K-H Kuck, P E Russell, H Lyr. BCPC, Alton, UK pp. 73-80

Sierotzki H, Wullschleger J, Gisi U (2000a). Point mutation in cytochrome b gene conferring resistance to strobilurin fungicides in *Erysiphe graminis* f. sp. *tritici* field isolates. *Pesticide Biochemistry and Physiology* **68,** 107-112

Sierotzki H, Parisi S, Steinfeld U, Tenzer I, Poirey S, Gisi U (2000b). Mode of resistance to respiration inhibitors at the cytochrome bc1 enzyme complex of *Mycosphaerella fijiensis* field isolates. *Pest Management Science* **56,** 833-841

Silva V L D, Loppes C A (1995). *Pseudomonas syringae* pv. tomato resistant to streptomycin and oxytetracycline in tomato plants treated or not with agricultural antibiotics. *Fitopatologia Brasileira* **20,** 80-84

Sisler H D (1971). Mode of action of benzimidazole fungicides. *Proceedings of the 2nd International Congress of Pesticide Chemistry IUPAC, Tel-Aviv,* p. 323

Sitton J W, Pierson C F (1982). Interaction and control of Alternaria stem decay and blue mold in Anjou pears. *Phytopathology* **72,** 1008 (Abstract)

Skinner W, Bailey A, Renwick A, Keon J, Gurr S, Hargreaves J (1998). A single amino-acid substitution in the iron-sulphur protein subunit of succinate dehydrogenase determines resistance to carboxin in *Mycosphaerella graminicola. Current Genetics* **34**, 393-398

Smiley R W, Howard, R J (1976). Tolerance to benzimidazole derivative fungicides by *Fusarium roseum* on Kentucky blue grass turf. *Plant Disease Reporter* **60,** 91 – 94

Smith F D, Phipps P M, Stipes R J, Brenneman T B (1995). Significance of insensitivity of *Sclerotinia minor* to iprodione in control of Sclerotinia blight of peanut. *Plant Disease* **79,** 517-523

Source: www.frac.info
January 2013

Spalding D H (1982). Resistance of Mango pathogens to fungicides used to control postharvest diseases. *Plant Disease* **66,** 1185-1186
Spotts R A, Cervantes L A (1995). Copper, oxytetracycline and streptomycin resistance of *Psedomonas syringae* pv. *syringae* strains from pear orchards in Oregon and Washington. *Plant Disease* **79,** 1132-1135
Staub T, Sozzi D (1981). Résistance au métalaxyl en pratique et les conséquences pour son utilisation. *Phytiatrie – Phytopharmacie* **30,** 283 – 291
Stanis V F, Jones A L (1985). Reduced sensitivity to sterol inhibiting fungicides in field isolates of *Venturia inaequalis. Phytopathology* **75,** 1098 – 1101
Starndberg J O (1984). Efficacy of fungicides against persistence of *Alternaria dauci* on carrot seed *Daucus carota. Plant Disease* **68,** 39-42
Staunton W F, Kavanagh T (1975). Resistance of fungal pathogens to benomyl in Ireland and results of alternative spray programmes for disease control. *Proceedings of the British Insecticide and Fungicide Conference* **8,** 1-4
Steekelenburg N A M van (1973). *Ascochya bij chrysant*; resistent geworden tegen benomyl (Benlate). *Vakbl. Bloemistrerij* **28,** 13
Steekelenburg N A M van (1987). Resistance to benzimidazole and dicarboximide fungicides in *Botrytis cinerea* and *Didymella bryoniae* in cucumbers in the Netherlands. *Medelingen van de Faculteit Landbouwwetenschappen Universiteit Gent* **52,** 875-880
Stehmann C, De Waard M A (1996). Sensitivity of populations of *Botrytis cinerea* to triazoles, benomyl and vinclozolin. *European Journal of Plant Pathology* **102,** 171-180
Stein J M, Kirk W W (2003). The generation and quantification of resistance to dimethomorph in *Phytophthora infestans. Plant Disease* **88,** 930 - 934
Steinfeld U, Sierotzki H, Parisi S, Gisi U (2002). Comparison of resistance mechanisms to strobilurin fungicides in *Venturia inaequalis*. In: *Modern Fungicides and Antifungal Compounds III.* Eds. H-W DEhne, U Gisi, K-H Kuck, P E Russell, H Lyr. AgroConcept GmbH, Bonn. pp. 167-176
Steva H, Cartolaro P, Gomes da Silva M T (1990). Tolerance of powdery mildew of SBI fungicides: situation for 1989. *Phytoma* **419,** 41 – 44
Stevenson K L, Langston D B, Seebold K W (2002). Resistance to azoxystrobin in the gummy stem blight pathogen in Georgia. *Phytopathology* **92,** S79
Stevenson K L, Langston D, Sanders B F (2008). Baseline sensitivity and evidence of resistance to boscalid in *Didymella bryoniae* *Phytopathology* **98**:S151
Stover R H (1979). Field observations on benomyl tolerance in ascospores of *Mycosphaerella fijiensis* var. *difformis*. *Transactions of the British Mycological Society* **72,** 518 – 519
Suta V, Radulescu M (1986). Investigations on the integrated control of apple diseases in the orchards with biotypes of *Venturia inaequalis* and *Podosphaera leucotricha* (Ell *et* Ev.) Salm resistant to benzimidazolyc and triforine fungicides. *Hortscience* **23,** 747 (abstract)
Szkolnik M, Gilpatrick J D (1969). Apparent resistance of *Venturia inaequalis* to dodine in New York apple orchards. *Plant Disease Reporter* **53**, 861 - 864
Szkolnik M, Gilpatrick J D (1971). Resistance of *Venturia inaequalis* to N dodecyl guanidine acetate. *Phytopathology* **61,** 132

Source: www.frac.info
January 2013

T

Taga M, Nakagawa H, Tsuda M, Ueyama A (1979). Identification of 3 loci controlling kasugamycin resistance in *Pyricularia oryzae. Phytopathology* **69,** 463-466

Takagaki M, Kaku K, Watanabe S, Kawai K, Shimizu T, Sawada H, Kumakaru K, Nagayama K (2004). Mechanism of resistance to carpropamid in *Magnaporthe grisea. Pest Management Science* **60,** 921-926

Tamura O (2000). Fluazinam resistance in leguminous *Botrytis cinerea* and resistance management. *Abstracts of the 10th. Symposium of Research Committee on Fungicide Resistance* pp 7-16

Tanaka F, Saito I, Miyajima K, Tsuchiya S, Tsuboki K (1983). Occurrence of thiophanate methyl tolerant isolates of *Fusarium nivale* synonymy *Gerlachia nivalis* a causal fungus of snow mold of winter wheat in Japan. *Annals of the Phytopathological Society of Japan* **49,** 565 – 566

Taylor R J, Sales B, Secor G A, Rivera V, Gumestad N C (2002). Sensitivity of North American isolates of *Phytophthora erythroseptica* and *Pythium ultimum* to mefenoxam (metalaxyl). *Plant Disease* **86,** 797 – 802

Thanassoulopoulos C C, Giannopilitis C N, Kitsos G T (1970). Evaluation of sensitiveness and development of resistance of *Fusarium oxysporum* f.sp. *lycopersici* to benomyl. *Phytopathologischea Zeitschrift* **70,** 114-120

Tivoli B, Deltour A, Molet D, Bedin P, Jouan B (1986). Isolation of thiabendazole resistant strains of *Fusarium roseum* var *sambucinum* from potato tubers. *Agronomie* **6,** 219 – 224

Tominaga A, Kobayashi Y (1978). Kasugamycin resistant mutants of *Bacillus subtilis. Journal of Bacteriology* **135,** 1149-1150

Tomita Y, Ishii H (1998). Reduced sensitivity to fenarimol in Japanese field strains of *Venturia nashicola. Pesticide Science* **54,** 150 – 156

Top Agrar (2009). Online article in Top Agrar December 2009. www.topagrar.com

Tramier R, Bettachini A (1974). A strain of *Fusarium oxysporum* f sp. *dianthi* resistant to systemic fungicides. *Annales de Phytopathologie* **6,** 231 – 236

Tremblay D M, Talbot B G, Carisse O (2003). Sensitivity of *Botrytis squamosa* to different classes of fungicides. *Plant Disease* **87,** 573-578

U

Uesugi Y (1981). Resistance to fungicides in *Pyricularia oryzae. Journal of pesticide Science* **6,** 239-246

V

Valaskova E (1983). The influence of various carbon and nitrogen sources on mycelium growth and resistance stability in a benomyl tolerant strain of *Fusarium oxysporum* f sp. *tulipae. Sbornik UVTIZ (Ustav Vedeckotechnickych Informaci pro Zemedelstvi) Ochrana Rostlin* **19,** 251 -260

Van Bruggen A H C, Arneson P A (1984). Resistance in *Rhizoctonia solani* to tolclofos methyl. *Netherlands Journal of Plant Pathology* **90,** 95 – 106

Vargas J M Jr. (1973). A benzimidazole resistant strain of *Erysiphe graminis. Phytopathology* **63,** 1366 – 1368

Source: www.frac.info
January 2013

Vargas J M Jr., Golembiewski R, Detweiler A R (1992). Reduced sensitivity of *Sclerotinia homoeocarpa* to DMI fungicides. *Phytopathology* **82,** 1069
Veverke K (1983). Resistance of *Verticillium albo-atrum* Reinke et Bert. to benomyl and trimorfamid. *Zbl. Mikrobiol.* **138,** 565-568
Viljanen-Rollinson S L H, Marroni M V, Butler R C (2007). Reduced sensitivity to carbendazim in isolates of *Botrytis allii*. *New Zealand Plant Protection* **60** 108-113
Vincelli P, Dixon E (2002). Resistance to QoI (strobilurin-like) fungicides in isolates of *Pyricularia grisea* from perrenial ryegrass. *Plant Disease* **86,** 235-240
Vitale A, Aiello D, Castello I, Polizzi G (2009). First report of Benzimidazole resistant isolates of *Cylindrocladium scoparium* in Europe. *Plant Disease* **93** 110

W

Walker A S, Auclair C, Gredt M, Leroux P (2009). First occurrence of resistance to strobilurin fungicides in *Microdochium nivale* and *Microdochium majus* from French naturally infected wheat grains. *Pest Management Science* **65** 906-915
Walsh R C, Sisler H D (1981). Cross resistance patterns of fenarimol resistant isolates of *Ustilago maydis. Phytopathology* **71,** 771 – 772
Weber R W S, Palm G (2010). Resistance of storage rot fungi *Neofabraea perennans, N. alba, Glomerella acutata* and *Neonectria galligena* against thiophanate-methyl in Northern German apple production. *Journal of Plant Diseases and Protection.* **117,** 185-191
Whan J H (1976). Tolerance of *Sclerotinia fructicola* to benomyl. *Plant Disease Reporter* **60,** 200 – 201
White G A, Georgopoulos S G (1986). Thiophene carboxamide fungicides structure activity relationships with the succinate dehydrogenase complex from wild type and carboxin resistant mutants of *Aspergillus nidulans. Pesticide Biochemistry and Physiology* **25,** 188-204
White J G, Stanghellini M E, Ayoubi L M (1988). Variation in the sensitivity to metalaxyl of *Pythium* spp isolated from carrot and other sources. *Annals of Applied Biology* **113,** 269 – 278
Whiteside J O (1980a). Detection of benomyl tolerant strains of *Elsinoe fawcetti* in Florida citrus groves and nurseries. *Plant Disease* **64,** 871-872
Whiteside J O (1980b). Tolerance of *Mycosphaerella citri* to benomyl in Florida USA citrus groves. *Plant Disease* **64,** 300 – 302
Wicks T (1977). Tolerance to benzimidazole fungicides in blue mold (*Penicillium expansum)* on pears. *Plant Disease Reporter* **61,** 447-449
Wilcox W F, Burr J A, Riegel D G, Wong F P (2003). Practical resistance to QoI fungicides in New York populations of *Uncinula necator* associated with quantitative shifts in pathogen sensitivities. *Phytopathology* **93,** S90
Wild B L (1983). Double resistance by citrus green mold *Penicillium digitatum* to the fungicides guazatine and benomyl. *Annals of Applied Biology* **103,** 237 – 242
Wise K A, Bradley C A, Pasche J S, Gudmestad N C (2009). Resistance to QoI fungicides in *Ascochyta rabiei* from chickpea in the Northern Great Plains. *Plant Disease* **93** 528-536

Source: www.frac.info
January 2013

Wong F P, De la Carda K A, Hernandez-Martinez R, Midland S L (2008). Detection and characterization of benzimidazole resistance in California populations of *Colletotrichum cereale. Plant Disease* **92**, 239-246

Wong S P (2003). Past, current and future challenges for fungicide resistance management for turfgrass pathogens. *Phytopathology **93** supplement6,* S114

Wright P J (2004). Resistance of *Peronospora destructor* (onion downy mildew) to metalaxyl fungicides. *New Zealand Plant Protection* **57,** 347. (Conference Proceedings)

Wu Y, Lu S, Huang S, Fu G, Chen L, Xie D, L Q, Cen Z (2011). Field resistance of *Phytophthora melonis* to metalaxyl in South China. *Weishengwu Xuebo,* **51,** 1078-1086

XYZ

Xiao C L**,** Kim Y K**,** Boal**,** R J (2011). First report of occurrence of pyrimethanil resistance in *Penicillium expansum* from stored apples in Washington State. *Plant Disease* **95**, 72

Yamada N, Motoyama T, Nakasako M, Kagabu S, Kudo T, Yamaguchi I (2004). Enzymatic characterisation of scytalone dehydratase Val75Met variant found in melanin biosynthesis dehydratase inhibitor (MBI-D) resistant strains of the rice blast fungus. *Bioscience Biotechnology and Biochemistry* **68,** 615-621

Yamaguchi J, Inada M, Matsuzaki M (2000). Occurrence of DMI fungicide resistant isolates of *Mycovellosiella nattrassii* Deighton, causal fungus of leaf mold of eggplant. *Japanese Journal of Phytopathology* **66,** 78 – 84

Yamaguchi J., Kuchiki F., Hirayae K., So K. (2002), Decreased effect of carpropamid for rice blast control in the west north area of Saga prefecture in 2001. *Japanese. Journal of Phytopathology* **68**: 261 (Abstr.).

Yano K, Kawada Y (2003). Occurrence of strobilurin-resistant strains of *Mycovellosiella nattrassii*, causal fungus of leaf mold of eggplants. *Japanese Journal of Phytopathology* **69,** 220-223

Yin Y, Liu X, Li B, Ma Z (2009). Characterization of sterol demethylation inhibitor resistant isolates of *Fusarium asiaticum* and *F. graminearum* collected from wheat in China. *Phytopathology* **99** 487-497

Yin Y N, Kim Y K, Xiao C L (2011). Molecular characterisation of boscalid resistance in field isolates of *Botrytis cinerea* from apple. *Phytopathology* **101,** 986-995

Young D H, Kemmitt G M, Owen J (2005). A comparative study of XR-539 and other oomycete fungicides: Similarity to dimethomorph and amino acid amides in its mechanism of action. *In*: Modern Fungicides and Antifungal Compounds IV. Eds. H-W Dehne, U Gisi, K-H Kuck, P E Russell, H Lyr. BCPC, Alton, UK pp. 145-152

Young D H, Spiewak S L, Slawecki R A (2001). Laboratory studies to assess the risk of development of resistance to zoxamide. *Pest Management Science* **57,** 1081-1087

Yu K-S (1981). Studies on the fungicide resistance of citrus blue mold fungus. *Plant Protection Bulletin (Taichung)* **23,** 193 – 200

Yuan S K, Liu X L, Si N G, Dong J, Gu B G, Jiang H (2006). Sensitivity of *Phytophthora infestans* to flumorph: *in vitro* determination of baseline sensitivity and the risk of resistance. *Plant Pathology* **55,** 258-263

Source: www.frac.info
January 2013

Zhang C Q, Zhu G N, Ma Z H, Zhou M G (2006). Isolation, characterization and preliminary genetic analysis of laboratory tricyclazole resistant mutants of the rice blast fungus, *Magnaporthe grisea. Journal of Phytopathology (Berlin)* **154,** 392 – 397

Zhao Zhi-hua, Mang Xi-ming, Fan Jie-ru, Liu Liang, Lfu Xi-Ii (2007). Effect of prochloraz on growth and development of prochloraz sensitive strain and its resistant mutants in *Fusarium fujikuroi. Nongyaoxue Xuebao* **9** 251-256

Zheng D, Olaya G, Koller W (2000). Characterization of laboratory mutants of *Venturia inaequalis* resistant to the strobilurin related fungicide kresoxim-methyl. *Current Genetics* **38,** 148-155

Zhu Zhi-feng, Pan Hong-yu, Zhang Hao, jiang Hui, Yuan Shan-kui, Qing-ping Yan (2006). Induction and characteristics of mutants of *Phytophthora drechsleti* resistant to etridiazole. Nongyaoxue xuebao **8** (4) 323-326 (Chinese)

Ziogas B N, Markoglou A N, Tzima A (2002). A non-mendelian inheritance of resistance to strobilurin fungicides in *Ustilago maydis. Pest Management Science* **58,** 908-916

Ziogas B N, Markoglou A N, Malandrakis A A (2003). Studies on the inherent resistance risk to fenhexamid in *Botrytis cinerea. European Journal of Plant Pathology* **109,** 311-317

Reference 3

Footnotes: 7 & 16

Fungicide Resistance Management

John Damicone
Extension Plant Pathologist

Damon Smith
Extension Plant Pathologist

Oklahoma Cooperative Extension Fact Sheets are also available on our website at:
http://osufacts.okstate.edu

Fungicides are important tools for managing diseases in many crops. Unlike insecticides and some herbicides which kill established insects or weeds, fungicides are most commonly applied to protect healthy plants from infection by fungal plant pathogens. To be effective, fungicides must be applied before infections become established and in a sufficient spray volume to achieve thorough coverage of the plant or treated area. Protection from fungicides is temporary because they are subject to weathering and breakdown over time. They also must be reapplied to protect new growth when disease threatens. Poor disease control with fungicides can result from several causes including insufficient application rate, inherently low effectiveness of the fungicide on the target pathogen, improper timing or application method, and excessive rainfall. Resistance (lack of sensitivity) to fungicides in fungal pathogens is another cause of poor disease control. The development of fungicide resistance is influenced by complex interactions of factors such as the mode of action of the fungicide (how the active ingredient inhibits the fungus), the biology of the pathogen, fungicide use pattern, and the cropping system. Understanding the biology of fungicide resistance, how it develops, and how it can be managed is crucial for ensuring sustainable disease control with fungicides.

The problem of fungicide resistance became apparent following the registration and widespread use of the systemic fungicide (see fungicide mobility below) benomyl (Benlate) in the early 1970s. Prior to the registration of benomyl, growers routinely applied a protectant fungicide (see fungicide mobility below) such as maneb, mancozeb, or copper to control diseases without experiencing resistance problems. A distinct advantage of benomyl over the protectant fungicides was its systemic activity. In addition to protecting plants from infection, systemic activity conferred rainfastness and provided disease control when applied after the early stages of infection. Superior disease control was often achieved with benomyl compared to the protective dithiocarbamates. However, benomyl differed from the dithiocarbamates in its site-specific mode of action (see Fungicide Groups and Mode of Action below) which was readily overcome by several fungal pathogens. Resistance problems appeared a few years after benomyl was introduced where the fungicide was used intensively. Sudden control failures occurred with diseases such as powdery mildew, peanut leaf spot, and apple scab.

Many of the fungicides developed and registered since the introduction of benomyl also are systemic, have a site-specific mode of action, and are at increased risk for resistance problems. Fungicide resistance is now a widespread problem in global agriculture. Fungicide resistance problems in the field have been documented for more than 100 diseases (crop - pathogen combinations), and within about half of the known fungicide groups. Many more cases of resistance are suspected but have not been documented. While resistance risks with many of fungicides may not be as great as with benomyl, strategies to manage the resistance risk have been developed and implemented to avoid unexpected control failures and sustain the usefulness of new products. As a result of resistance management strategies, fungicides within all mode of action groups remain useful disease management tools in at least some cropping systems. The purpose of this bulletin is to describe the resistance phenomenon, identify resistance risks in the different fungicide groups, and to provide general guidelines for managing resistance. Since this fact sheet was first written, many new fungicides have been registered, and mode of action groups and specific resistance management strategies are now specified on fungicide labels. The listing of fungicides by mode of action group here is useful for identifying appropriate fungicides for use in tank mixtures and application schedules as part of the recommended resistance management programs.

Fungicide Mobility

Understanding the mobility of fungicides on and in treated plants, and how various fungicides are classified based on mobility is important when making decisions pertaining to the selection of the best fungicide for a particular disease and its optimal application timing. Fungicides can be classified into two basic mobility groups: protectant or penetrant. Regardless of its mobility characteristics, no fungicide will be highly effective after the development of disease symptoms and pathogen reproduction (spore production). Fungicides can slow or stop the development of new symptoms if applied in a timely fashion, but fungicides will not cure existing disease symptoms. Therefore, understanding fungicide mobility, fungicide mode of action, and the biology of the target pathogen are important so fungicide applications are made before the disease becomes established and more difficult to control.

Protectant fungicides are active on the plant surfaces where they remain after application. There is no movement of the fungicide into the plant. Because they remain on the plant surface, protectant fungicides loose activity after being washed off the plant and must be re-applied to new growth that develops after application. Protectant fungicides typically prevent spore germination, therefore they must be applied prior to infection and have no effect once the fungus grows into the plant resulting in infection.

Penetrant fungicides are absorbed into plants following application. Because these fungicides are absorbed into plants, they are generally considered systemic fungicides. However, penetrant fungicides have different degrees of systemic movement once inside the plant. Some fungicides are 'locally systemic,' only moving a short distance such as through a few layers of plant cells. Fungicides that move from one side of a leaf to other have 'translaminar' movement. Translaminar and locally systemic fungicides are not transported throughout the

plant. Highly mobile fungicides are either 'xylem-mobile' or 'true systemics.' Xylem-mobile fungicides move upward in plants and outward to the periphery of leaves with water through the xylem, the water conducting tissue of the plant. True systemic fungicides move both upward through the xylem, and downward through the phloem, the food conducting tissue of the plant. Few if any fungicides are fully systemic. Unlike protectant fungicides, penetrant fungicides are rain fast within a few hours of application and may require a less thorough application coverage to be effective. In addition, many penetrant fungicides inhibit fungal growth and sporulation and can be effective when applied after the early stages of infection. Regardless of the level of systemic movement, penetrant fungicides have limited 'curative' ability. Generally they only stop or slow infections within the first 24- to 72-hour period following fungal penetration into the plant. Therefore, penetrant fungicides must be applied before or shortly after infection, and are ineffective on existing symptoms. Both protectant and penetrant fungicides provide good disease control when applied before infection and are best applied on a preventive schedule.

Development of Fungicide Resistance

Resistance is a genetic adjustment by a fungus that results in reduced sensitivity to a fungicide. Reduced sensitivity is thought to be a result of genetic mutations which occur at low frequencies (one in a million or less) or of naturally occurring sub-populations of resistant individuals. Individuals in a fungal population may consist of the mycelium (the body of a fungus), sclerotia (large survival structures), spores (small reproductive structures), or the nucleus of single cells capable of reproduction and spread. The resistance trait may result from single gene or multiple gene mutations (see build-up of resistance below). Single-gene mutations that confer resistance to site-specific fungicides are more likely to develop than the simultaneous occurrence of mutations in multiple genes needed to confer resistance to multi-site inhibiting fungicides. Mechanisms of resistance differ depending on the mode of action, but include alteration of the target site, reduced fungicide uptake, active export of the fungicide outside fungal cells, and detoxification or breakdown of the fungicide.

The level of resistance to a fungicide can be measured in the laboratory by exposing a collection of members of a field population to the fungicide and measuring toxicity response. Toxicity responses are usually measured as inhibition of fungus growth, spore germination, or actual plant infection in cases where the fungus cannot be cultured. The effective concentration which inhibits growth, germination, or infection by 50 percent (EC_{50}) is then calculated for each sampled individual much in the same way an LD_{50} (50 percent lethal dose) is calculated for assessing the acute toxicity of a pesticide to rats or mice. Where many members of a population are sampled and screened, a range of sensitivity (or resistance) to the fungicide is usually observed. The frequency distribution of the sensitivity of individuals in the population is usually normal or bell-shaped, typical of many biological responses in nature (Figure 1). Where the fungicide is newly introduced or where the risk of resistance is low, the population is distributed over a sensitive range. However, a distribution consisting of two distinct sub-populations also may occur where a small sub-population of resistant strains is present along with a larger sub-population of sensitive strains (Figure 1A).

Build-up of Resistance

Resistance in a population becomes important when the frequency of resistant strains builds up to dominate the population. The build-up of resistant strains is caused by repeated use of the fungicide which exerts selection pressure on the population. The fungicide selectively inhibits sensitive strains, but allows the increase of resistant strains. This shift toward resistance occurs at different rates, depending on the number of genes conferring resistance. When single gene mutations confer resistance, a rapid shift toward resistance may occur, leading to a population that is predominantly resistant and where control is abruptly lost (Fig. 1A). When multiple genes are involved, the shift toward resistance progresses slowly, leading to a reduced sensitivity of the entire population (Fig. 1B). The gradual shift with the multiple gene effect may result in reduced fungicide activity between sprays, but the risk of sudden and complete loss of control is low. It is difficult to clearly distinguish between sensitive and resistant sub-populations with field sampling during the early shifts towards reduced sensitivity because sensitivity responses overlap. Large numbers of individuals must be tested to identify the gradual type of resistance.

Assessing Resistance Risk

Many factors effect the development of resistance and its build-up in the field, which makes it difficult to predict the resistance risk for new fungicides. Despite resistance problems that have been identified following the introduction of some new fungicides, many examples can be cited where their use continues to be effective. Factors that must all be considered in assessing resistance risk include the properties of the fungicide, the biology of the pathogen, and the crop production system where the fungicide is used.

Fungicide Groups and Mode of Action

Fungicides are grouped by similarities in chemical structure and mode of action. Site-specific fungicides disrupt single metabolic processes or structural sites of the target fungus. These include cell division, sterol synthesis, or nucleic acid (DNA and or RNA) synthesis. The activity of site-specific fungicides may be reduced by single or multiple-gene mutations. The benzimidazole, phenylamide, and strobilurin groups are subject to single-gene resistance and carry a high risk of resistance problems. Other

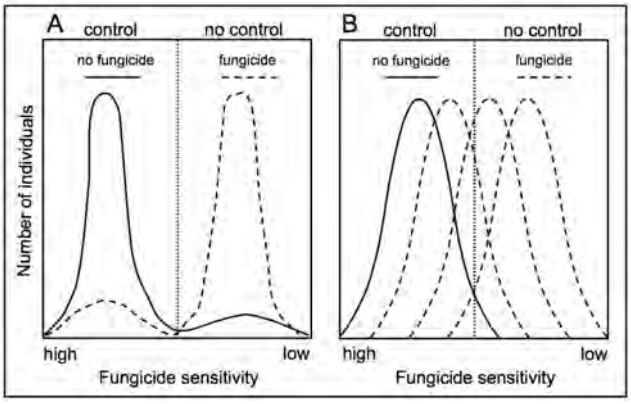


Figure 1. Depiction of the possible ways fungicide resistance develops in population of a fungal pathogen. A) Abrupt (qualitative) resistance development where an initially small, subpopulation of resistant strains is present before fungicide usage or develops as a result of a single gene mutation occurring at low frequency (solid line). Following selection pressure of fungicide use, the frequency of resistant individuals (broken line) becomes predominant and disease control is rapidly lost. B) Gradual (quantitative) resistance development arising from an accumulation of mutations in multiple genes that leads to reduced sensitivity. The initial population (solid line) is sensitive, but gradually shifts towards reduced sensitivity under the selection pressure of fungicide use (broken line).

fungicide groups with site-specific modes of action include dicarboximides and sterol demethylation inhibitors (DMIs), but resistance to these fungicides appears to involve slower shifts toward insensitivity because of multiple-gene involvement. Many of the site-specific fungicides also have systemic mobility. However, systemic mobility is not necessary for resistance development. Resistance problems have developed in the dicarboximide group and with dodine, which are protectant fungicides.

Multi-site fungicides interfere with many metabolic processes of the fungus and are usually protectant fungicides. Once taken up by fungal cells, multisite inhibitors act on processes such as general enzyme activity that disrupt numerous cell functions. Numerous mutations affecting many sites in the fungus would be necessary for resistance to develop. Typically, these fungicides inhibit spore germination and must be applied before infection occurs. Multi-site fungicides form a chemical barrier between the plant and fungus. The risk of resistance to these fungicides is low.

There are two codes currently used to classify fungicides by mode of action (Table 1). The mode of action group (A, B, etc.) refers to the general target site such as nucleic acid synthesis, cell wall synthesis, respiration, etc. Sub-groups (A1, A2, etc.) within a mode of action group refer to specific biochemical target sites of fungicide activity. The FRAC (Fungicide Resistance Action Committee) code is used on the fungicide label. The FRAC code refers to fungicides that have same site-specific mode of action and share the same resistance problems across members of the group (cross-resistance). FRAC groups are currently numbered from 1 to 43 in order of their introduction to the marketplace. FRAC groups and mode of action subgroups are mostly the same.

Fitness of Resistant Strains

Fitness is the ability to compete and survive in nature. Strains of pathogens resistant to some fungicides compete equally well with sensitive strains and are still present after the fungicide in question is no longer in use. For example, strains of *Cercospora arachidicola* which causes early leaf spot of peanut are still established in the southeastern U.S. where benomyl resistance was a problem more than 20 years ago. Therefore, fungicides with resistance problems cannot be successfully reintroduced into areas where resistant strains are highly fit. Fortunately, resistant strains are sometimes less fit than wild-type sensitive strains. This has been true for DMI resistance in powdery mildews and for dicarboximide resistance in Botrytis diseases. Unfit strains only compete well under the selection pressure of the fungicide. Thus, the resistance is at least partially reversible when the selection pressure of the fungicide is removed or minimized by using resistance management.

Fungicide Use Pattern

Frequent and exclusive usage of at-risk fungicides increases the risk of resistance problems. Selection pressure is increased where repeated applications are required for disease control as with many foliar diseases. Selection pressure and the risk of resistance are low for seed treatments and for many soilborne diseases which require only one or two applications per season. The method and rate of application may also impact resistance development. Poor disease control resulting from causes such as improper application timing or inadequate spray coverage may result in a need for a more intensive spray program and the exposure of more individuals to the fungicide. Using adequate rates in a manner that produces good disease control reduces the reproductive capacity of fungal pathogens, thus reducing selection pressure. Similarly, a preventive spray program is less risky than a rescue program because selection pressure is applied to fewer individuals. Finally, an increase in selection pressure results from an excessive number of applications where a real need is not justified.

Pathogen Biology

Fungal pathogens with high rates of reproduction are most prone to develop fungicide resistance. Because many individuals (usually spores) are produced by these fungi, more individuals are exposed to selection pressure and there is a greater probability of mutations that lead to reduced fungicide sensitivity. Foliar diseases produce thousands of spores on the surface of an individual leaf spot. Furthermore, these diseases typically have several reproductive cycles per season. Under selection pressure of a fungicide, resistant individuals may increase rapidly and dominate the population after several cycles of infection and reproduction.

Diseases with low reproduction rates generally complete only one life cycle per season. Soilborne pathogens produce fewer offspring per season than their foliar counterparts. Some soilborne diseases reproduce by forming seed-like survival structures called sclerotia. There may be fewer than a hundred sclerotia formed per plant. Where an at-risk fungicide is used for soilborne disease control, resistance development is likely to be slow because comparatively few individuals are exposed to selection pressure.

Crop Production Practices

Production practices that favor increased disease pressure also promote resistance development by increasing the number of individuals exposed to selection pressure. Pathogens reproduce at higher rates on susceptible varieties compared to resistant or partially resistant varieties. Selection pressure also may be reduced for resistant varieties because fewer applications should be needed for effective disease control. Inadequate or excessive fertilization with nitrogen may increase disease incidence in some crops. For example, early blight of potato and tomato and dollar spot of turfgrass are favored by nitrogen deficiency. Alternatively, the severity of spring dead spot of bermudagrass and some foliar diseases of wheat is increased with intensive nitrogen fertilization. Excessive irrigation or frequent irrigation with small amounts of water increases the incidence of many diseases by promoting disease spread, extended periods of leaf wetness, and high soil moisture.

Continuous cropping and poor sanitation practices promote severe early-season disease development. Closed cropping systems such as greenhouses are particularly prone to resistance problems because plants are grown in crowded conditions that may favor severe disease development, rapid spread, and high selection pressure. Permanently established plantings of perennial crops such as orchards, nurseries, and vineyards are particularly prone to resistance problems. Unlike annual crops where crop rotation can be practiced, many pathogens survive from year to year on plants and crop debris within permanent plantings resulting in a local pathogen population exposed to yearly selection pressures.

Resistance Management Strategies

Strategies for managing fungicide resistance are aimed at delaying its development. Therefore, a management strategy should be implemented before resistance becomes a problem. The only way to absolutely prevent resistance is to not use an at-risk fungicide. This is not a practical solution because many of the modern fungicides that are at risk for resistance problems provide highly effective, broad-spectrum disease control. By delaying resistance and keeping its level under control, resistance can be prevented from becoming economically important. Because practical research in the area of fungicide resistance management has been limited, many of the strategies devised are based in the theory of expected responses of a pathogen population to selection pressure. For the most part, evaluations of the effectiveness of these strategies have not been based on

Table 1. Fungicides registered in the United States grouped by mode of action and relative risk for developing resistance problems.

Mode of action	*Group* [1]	*Group name*	*Common name*	*Trade names*	*Mobility*[2]	*Uses* [3]	*Risk* [4]
Nucleic acid synthesis	A1 (4)	Phenylamide	metalaxyl	Allegiance, MetaStar, Apron	S	ST, F, S	H
			mefenoxam or metalaxyl-M	Ridomil Gold, Apron XL, Subdue, Ultra Flourish, Quali Pro	S	ST, F, S	H
Mitosis and cell division	B1 (1)	Benzimidazole	thiabendazole	Mertect	S	ST, PH	H
			thiophanate-methyl	Topsin M, Cleary's 3336, T-Methyl, OHP 6672, Thiophanate Methyl	S	ST, F, S	H
	B3 (22)	Benzamide	zoxamide	Gavel (+ mancozeb)	S	F	M
	B5 (43)	Acylpicolide	fluopicolide	Presidio	S	F,S	M
Respiration	C2 (7)	Carboxamide	carboxin	Vitavax	S	ST	L
			flutolanil	Contrast, Moncut, ProStar, Artisan (+ propiconazole)	S	ST, F, S	M
			boscalid	Endura, Emerald, Pristine (+ pyraclostrobin)	S	F, S	M
	C3 (11)	Strobilurin (Quinone outside Inhibitor (QoI))	azoxystrobin	Abound, Amistar, Heritage, Quadris, Protege, Dynasty, Quilt (+ propiconazole)	S	F, S, ST	H
			famoxidone	Tanos (+ curzate)	S	F	H
			fenamidone	Reason	S	F	H
			fluoxastrobin	Evito, Disarm	S	F, S	H
			kresoxim-methyl	Cygnus, Sovran	S	F	H
			pyraclostrobin	Cabrio, Insignia, Headline, Pristine (+ boscalid)	S	F, S	H
			trifloxystrobin	Flint, Compass, Gem, Trilex, Absolute (+ tebuconazole), Stratego (+ propiconazole)	S	F, S, ST	H
	C4 (21)	Quinone inside Inhibitor (QiI)	cyazofamid	Ranman	S	F	M
	C5 (29)	Dinitroaniline	fluazinam	Omega	P	F, S	L
	C6 (30)	Organo tin	triphenyl tin hydroxide	Super Tin, Agri Tin	P	F	L
Amino acids and proteins	D1 (9)	Anilino-Pyrimidine	cyprodinil	Vanguard, Switch (+ fludioxanil)	S	F	M
			pyrimethanil	Scala	S	F	M
	D4 (25)	Antibiotic (bactericide)	streptomycin	Agri-Mycin, Streptomycin, Firewall	P	ST, F	H
	D5 (41)	Antibiotic (bactericide)	oxytetracycline	Mycoshield, Flameout	P	F	H
Signaling	E1 (13)	Quinoline	quinoxyfen	Quintec	P	F	M
	E2 (12)	PhenylPyrrole	fludioxonil	Maxim, Scholar, Medallion, Switch (+ cyprodinil)	P	ST, F, PH	L-M
Lipids and membranes	F1 (2)	Dicarboximide	iprodione	Rovral, Chipco 26019, Iprodione, Chipco 26GT	P	F, S	M-H
			vinclozolin	Ronilan, Curalan	P	F, S	M-H
	F3 (14)	Aromatic Hydrocarbon	chloroneb	Nu-Flow D, Nu-Flow ND	P	ST	L
			dichloran	Botran	P	F, S, PH, ST	L-M
			PCNB	Terraclor, Turfcide	P	ST, S	L
			etridiazole	Terrazole, Terramaster	P	S	L-M
	F4 (28)	Carbamate	propamocarb HCl	Previcur Flex, Banol	S	F, S	L-M
	F5 (40)	Carboxylic Acid Amide	dimethomorph	Acrobat, Forum	S	F	L-M
			mandipropamid	Revus			
Sterol synthesis	G1 (3)	Demethylation Inhibitor (DMI)	cyproconazole	Alto, Quadris Xtra (+azoxystrobin)	S	F	
			fenarimol	Rubigan	S	F, S	M
			imazalil	Flo-Pro IMZ, Nu-Zone, Fecundal	S	ST, PH	L
			difenconazole	Dividend, Revus Top (+ mandipropamid)	S	ST, F	L-M

Table 1. continued.

Mode of action	*Group* [1]	*Group name*	*Common name*	*Trade names*	*Mobility* [2]	*Uses* [3]	*Risk* [4]
	G1 (3)	DMI (cont'd)	fenbuconazole	Enable, Indar	S	F	M
			myclobutanil	Nova, Rally, Eagle, Systhane, Laredo	S	F, S	M
			metconazole	Caramba, Quash	S	F,S	M
			propiconazole	Tilt, Orbit, Banner Maxx, Propiconazole, Propimax, Bumper, Propensity, Quilt (+ azoxystrobin), Stratego (+ trifloxystrobin)	S	F, S	M
			prothioconazole	Proline, Provost (+ tebuconazole)	S	F,S	M
			tebuconazole	Folicur, Raxil, Muscle, Trisum, Tebuzol, Orius, Elite, Absolute (+ trifloxystrobin)	S	F, S, ST	M
			tetraconazole	Domark, Eminent	S	F	M
			triadimefon	Bayleton	S	F, S	M
			triadimenol	Baytan	S	ST	L
			triflumizole	Procure, Terraguard	S	F, S	M
	G3 (17)	Hydroxyanilide	fenhexamid	Elevate, Captevate (+ captan)	P	F	L-M
Cell wall synthesis	H4 (19)	Polyoxins	polyoxin	Endorse	S	F, S	M
Plant defense activator	P1 (P)	Benzo-thiadiazole	acibenzolar-S-methyl	Actigard, Blockade	S	F	L
Unknown	U1 (27)	Cyanoacetamideoxime	cymoxanil	Curzate, Tanos (+ famoxadone)	S	F	M
	U2 (33)	Phosphonate	fosetyl-AL	Aliette, Legion, Chipco Signature	S	F	L
			phosphorous acid	Phostrol, AgriFos	S	F	L
			potassium phosphite	Fosphite, Prophyt	S	F	L
Multi-site activity	M1 (M1)	Inorganic	copper salts	Kocide, Cuprofix, Tenn-Cop, Basic Copper, Champ, Champion, Nu-Cop, Copper-Count-N	P	F	L
	M2 (M2)	Inorganic	sulfur	Microthiol, Sulfur, Super Six, Thiolux, Thiosperse	P	F	L
	M3 (M3)	Dithiocarbamate	ferbam	Ferbam	P	F	L
			mancozeb	Dithane, Penncozeb, Manzate, Fore, Mankocide (+ copper)	P	F, ST	L
			maneb	Maneb, Manex, Pentathlon	P	F, ST	L
			metiram	Polyram	P	F	L
			thiram	Thiram, Defiant	P	F, ST	L
			ziram	Ziram	P	F	L
	M4 (M4)	Phthalimide	captan	Captan, Captec	P	F, ST	L
	M5 (M5)	Chloronitrile	chlorothalonil	Bravo, Equus, Echo, Daconil, Chloronil, Chlorothalonil, Initiate, Concord, Spectro	P	F, S	L
	M7 (M7)	Guanadine	dodine	Syllit, Dodine	P	F	M

[1] Subgroups represent specific target sites within a mode of action, cross-resistance may occur within subgroups, FRAC group is in parenthesis. FRAC code is based on time of product registration and potential for cross-resistance within subgroups.

[2] P=protectant, S=systemic or penetrant.

[3] S=soilborne diseases, F=foliar diseases, ST=seed treatment, PH=post-harvest treatment.

[4] The resistance risk is assigned based on the worst case-scenario. For example, dicarboximide resistance is serious for some Botrytis diseases, but resistance problems have not developed with other uses. Seed treatment uses are considered low-risk regardless of he fungicide's properties.

research, but rather on observations made where the fungicides have been used commercially on a large scale.

Specific strategies for resistance management vary for the different fungicide groups, the target pathogen(s), and the crop. However, some strategies are generally effective (Table 2). Resistance management should integrate cultural practices and optimum fungicide use patterns. The desired result is to minimize selection pressure through a reduction in time of exposure or the size of the population exposed to the at-risk fungicide. Probably the most important aspect of optimizing use patterns is the deployment of tank mixtures and alternating sprays of the at-risk fungicide with a fungicide from a different mode of action group. The comparative merits of tank-mixing compared to alternating sprays have been debated. Some theorize that tank-mixing reduces selection pressure only when the partner fungicide is highly effective and good coverage is achieved. Alternating fungicides is thought to act by reducing the time of exposure. In practice, examples can be cited for the effectiveness of both approaches. Both practices are more effective when cultural practices are implemented to reduce disease pressure. The alternation of blocks of more than one spray is probably less effective in resistance management than the other use patterns. For example, a block of four continuous sprays of the DMI fungicide tebuconazole is recommended at mid-season for peanut disease control. Despite the use of at least one application of a non-DMI fungicide before and after the 4-spray block, resistance to tebuconazole in both early and late leaf spot diseases became a widespread problem in less than 10 years.

Table 2. Cultural practices and fungicide use patterns that reduce disease pressure and selection for fungicide resistance.

Strategy	*Result*
Cultural practices	
use resistant varieties	lower disease incidence and rate of increase
maintain proper soil fertility	reduces disease incidence
avoid sites with high disease pressure	avoids high selection
crop rotation	reduces initial pathogen population
sanitation	reduces initial pathogen population
Fungicide use patterns	
use only when justified	avoids unnecessary selection
use protectively	hits small populations
achieve good spray coverage	reduces populations exposed to selection
use tank mixes with protectants	reduces populations exposed to selection
alternate fungicides from different fungicide groups	reduces selection time
do not use soil applications against foliar diseases	reduces selection time

The proper choice of a partner fungicide in a resistance management program is critical. Generally, good partner fungicides are multi-site inhibitors that have a low resistance risk (e.g. chlorothalonil, mancozeb, etc.) and are highly effective against the target pathogen. However, the use of an unrelated at-risk fungicide with no potential for cross-resistance problems also may be effective. Specific resistance management strategies will be discussed for fungicide groups with the greatest history and/or risk for resistance problems.

Benzimidazoles (FRAC Group 1; Mode of Action Sub-Group B1)

Benzimidazoles are site-specific fungicides which interfere with cell division. They have systemic mobility and have activity on many pathogens except water molds (e.g. Pythium and Phytophthora) and darkly pigmented fungi (e.g. Alternaria). Research has demonstrated that benzimidazole resistant strains may be present at low frequencies in nature, even in the absence of fungicide exposure. Under selection pressure, resistance development is abrupt and rapid (Figure 1A). Resistant strains cannot be controlled by increasing the application rate or by shortening the spray interval. Resistant strains are often fit and competitive in nature even without selection pressure. Therefore, some populations have remained resistant where benzimidazole use has been discontinued for 10 years. Resistance to benzimidazoles has been documented for more than 60 diseases and cross-resistance exists within this fungicide group. Benzimidazole resistance has received less recent attention because the fungicide benomyl is no longer registered in the U.S. However, resistance management remains important for thiophanate-methyl, the other widely used benzimidazole fungicide.

Management of benzimidazole resistance relies on reducing the selection pressure by limiting fungicide exposure and using tank mixtures or alternating sprays with a fungicide with a low resistance risk (Table 3). Where multiple sprays are required for disease control, avoid using benzimidazoles alone for an extended period of time. In spite of the numerous resistance problems with benzimidazoles, there are also many examples where benzimidazoles have remained effective for more than 30 years with judicial use.

Strobilurins (FRAC Group 11; Mode of Action Sub-Group C3)

Strobilurin fungicides, also know as quinine-outside inhibitor (QoI) fungicides, are synthetic analogues of a naturally occurring compound produced by a wood rotting fungus. Strobilurins inhibit

Table 3. Guidelines for reducing the risk of resistance to benzimidazole fungicides (FRAC Group 1, Mode of Action Group B1).

1. Use cultural practices and pest management strategies that reduce disease pressure.
2. Do not exceed the allowable number of benzimidazole applications on the label.
3. Alternate or tank-mix benzimidazole applications with a fungicide from a different mode of action group. In tank-mixtures, both the benzimidazole and tank mix partner must be applied at their labeled rate.
4. Benzimidazoles should be use in preventive programs that keep disease pressure low.

respiration in fungal cells by targeting a protein (cytochrome bc-1) that is encoded by a gene in the mitochondria. The fungicides are broad-spectrum with activity against all the major types of fungal pathogens. Strobillurin fungicides penetrate plant leaves and move from one side of the leaf to the other. This translaminar mobility makes them rain-fast, but they lack true systemic movement in the plant compared to some other systemic fungicides. Strobilurins act on a broad range of fungal processes including spore germination, fungal growth, and reproduction (sporulation). Strobilurin fungicides have been registered on numerous crops because of their broad-spectrum activity and excellent human and environmental safety profiles. However, like the benzmidazoles, resistance developed shortly after their introduction in the late 1990s. Three different single-gene mutations have been identified that abruptly confer resistance (Figure 1A) that has been documented for more than 20 diseases. Resistant isolates are cross-resistant to all other strobilurin fungicides, but not to other mode of action groups including the closely related QiI (Group C4 or 21) fungicides.

Resistance management programs rely on reducing selection pressure by keeping disease pressure low, applying strobilurins in mixtures or alternation with fungicide from a different mode of action group, and limiting the number of applications per crop season (Table 4). Several strobilurin fungicides are marketed in pre-mixtures with non-strobilurin fungicides for use on certain crops.

Dicarboximides (FRAC Group 2; Mode of Action Sub-Group E3)

Dicarboximides inhibit both spore germination and fungal growth. Resistance is thought to arise by mutations. The frequency of resistant individuals and their level of resistance increase gradually with prolonged selection pressure (Figure 1B). Resistance to dicarboximide fungicides has been identified for more than 15 diseases including brown rot of stone fruits, gray mold (Botrytis) on several crops, and important turf grass diseases. Dicarboximide resistant strains of some pathogens are less fit to survive than sensitive strains. Reduced exposure of resistant strains to dicarboximide fungicides result in a decrease in the frequency of resistant strains and possibly an overall shift of the population back toward sensitivity. Thus, it has been possible to reintroduce dicarboximides into problem situations where resistance management has been implemented.

Table 4. Guidelines for reducing the risk of resistance to strobilurin fungicides (FRAC Group 11; Mode of Action Group C3).

1. Use integrated pest management and cultural practices known to reduce disease pressure. Strobilurin fungicides may be used in extension-sponsored disease advisory (disease forecasting) programs, which recommend application timing based on weather or risk factors favorable for disease development.
2. Limit the number of strobilurin applications to two to four per season depending on the crop as specified on the label.
3. Limit the number of sequential applications of strobilurin fungicide to one or two, depending on the crop and or region as specified on the label, before alternating with a fungicide from a different mode of action group.
4. Make preventative applications to keep disease pressure low.
5. Use pre-mixtures or tank mixtures of strobilurin fungicides with fungicides from a different mode of action group. The minimum labeled rates of each fungicide in the tank mix should be used.

Table 5. Guidelines for preventing and managing resistance to dicarboximide fungicides (FRAC Group 2, Mode of Action Group E3).

1. Use cultural practices that reduce the pathogen population.
2. Limit the number of dicarboximide applications to a maximum of 2-3 per season and maintain regular prolonged times without exposure to dicarboximides.
3. Tank-mix or alternate dicarboximide applications with an effective non-dicarboximide fungicide having a low resistance risk. Dicarboximide fungicides applied in tank mixtures count toward season totals.
4. Apply adequate rates as recommended on the label.

The primary goal of resistance management strategies for dicarboximides is to limit selection time (Table 5). Delay the first application as long as possible by using early-season applications of a protectant fungicide. This allows the deployment of dicarboximides at a time when the population of resistant strains is potentially the lowest. The possibility of resistance problems is greatest where dicarboximides are used frequently and exclusively. The number of applications made to a particular site should not exceed three per season. This applies to multiple crops grown in the same field. Resistance problems are likely to be manifested by a partial loss of control and a need for a closer spray interval. There is evidence that cross-resistance exists between members of this group and one dicarboximide should not be replaced with another where resistance is a problem. Dicarboximide resistance appears to be a manageable problem. These fungicides have remained useful for control of soilborne diseases and have been successfully reintroduced into cropping systems where resistance problems have arisen.

Demethylation Inhibitors (FRAC Group 3; Mode of Action Sub-Group G1)

Demethylation inhibitor (DMI) fungicides (Table 1) are site-specific fungicides that disrupt the synthesis of sterols. Sterols are compounds required for growth of many plant pathogenic fungi. DMIs are a large group of systemic fungicides that have a broad range of activity against many types of foliar and soilborne diseases except for those caused by the water molds. Resistance development is similar to the dicarboximides. Typically, resistance develops gradually and is at first difficult to detect (Figure 1B). Resistant strains are thought to have reduced fitness; therefore, reduced selection pressure through the use resistance management strategies may partially shift the resistant populations back toward sensitivity. DMI resistance has been documented for more than 20 diseases including apple scab, powdery mildews, gray mold, and brown rot of stone fruit.

Management strategies rely on the use of adequate rates and limiting exposure by tank-mixing or alternating DMI applications with unrelated fungicides (Table 6). Using adequate application rates is important because mildly resistant strains can still be controlled. Avoid using DMI fungicides alone all season long. Cross resistance is also a problem within this group so replacement of one DMI with another is not practical. Premixtures of DMI fungicides with strobilurin or protectant fungicides are being marketed for many crops to improve the spectrum of diseases controlled and to comply with resistance management guidelines.

Phenylamides (FRAC Group 4; Mode of Action Sub-Group A1)

Phenylamides are highly systemic fungicides specifically used to control diseases caused by water molds. Such dis-

Table 6. Guidelines for preventing and managing resistance to demithylation inhibitor (DMI) fungicides (FRAC Code 3; Mode of Action Group G1).

1. Use available cultural practices and resistant varieties to reduce disease pressure.
2. Apply according to label directions and do not use less than the minimum label rate alone or in tank mixtures.
3. Do not exceed the maximum allowed amount of a single DMI fungicide per season. Extending the allowed amount of one DMI fungicide with another will increase the risk of resistance development.
4. Keep the disease pressure low by using a preventive application schedule.
5. DMI fungicides are not recommended for season-long use alone. Alternate sprays or blocks of sprays a fungicide from a different mode of action group, use tank mixes of DMI fungicides with an effective protective fungicide having a low resistance risk.

Table 7. Guidelines for preventing and managing resistance to phenylamide fungicides (FRAC Group 4; Mode of Action Group A1).

1. The phenylamides should be used in a preventive program to keep disease pressure low.
2. For foliar applications, phenylamides should be used in premixtures with an unrelated (non-phenylamide) fungicide.
3. Solo formulations for soil use should not be used for foliar diseases and mixtures rather than straight phenylamides should be used for seed treatments whenever possible.
4. Soil treatments of phenylamides should not be used against foliar diseases.
5. The number of phenylamide applications should not exceed two to four per crop and year.
6. Phenylamide sprays are recommended early in season or during the period of active vegetative growth of the crop prior to switching to a non-phenylamide product later in the season.

eases include damping off and root and lower stem rots caused Pythium and Phytophthora, and foliar diseases such as late blight, downy mildew, and white rust. Phenylamides inhibit fungal growth by disrupting RNA synthesis. Resistance problems with phenylamides, specifically metalaxyl, were observed shortly after their introduction where they were used exclusively and disease pressure was high. Resistance is governed by one or two genes and a low frequency of resistant individuals may exist in wild populations prior to use of these fungicides. Resistance can increase rapidly through selection of the naturally occurring strains (Figure 1A). Cross resistance occurs with other phenylamide fungicides, but not with fungicides from other mode of action groups. Both resistant and sensitive strains survive in the absence of phenylamide fungicide use and their levels tend to equilibrate over time. Resistance management is critical to limit the proportion of resistant strains in a population.

Resistance management for phenylamide fungicides is most important for foliar diseases such as late blights and downy mildews for which multiple sprays are required. Management relies heavily on the use of premixes of phenylamides with protectant fungicides and limiting selection pressure (Table 7). The manufacturer of metalaxyl-M markets premixes with mancozeb, copper, and chlorothalonil for use against foliar pathogens. Selection pressure is reduced by limiting the number of sprays per crop and year. The marketing of pre-mixes of metalaxyl-M with non-related protectant fungicides ensures compliance with a resistance management strategy.

Conclusions

Fungicide resistance is one of several possible causes of poor disease control. Fungicide resistance not only threatens the usefulness of individual of fungicides, but also the farm economy because of potential yield losses from poor disease control. Unfortunately, registrations are being lost for older broad-spectrum fungicides that have a low resistance risk. Many of the newer replacement fungicides are more selective in the number and types of diseases controlled and have site-specific modes of action making them more prone to resistance problems. Maintaining an array of effective fungicides is critical. Resistance management strategies should be recommended by crop advisors and implemented by growers to prolong the active life of at-risk fungicides. Fungicide groups have different levels of resistance risk. Risk assessment is critical for newly developed fungicides. Mode of action group and resistance management strategies are now clearly included on the registration labels of most site-specific fungicides. However, it is difficult to predict the actual risk of resistance because of many interacting factors. Experience with resistance indicates that resistance problems are often manageable. Monitoring resistance levels in pathogen populations is essential for assessing risk and evaluating management practices. Unfortunately, there is no coordinated monitoring effort in place and growers will generally have to rely on proven methods of resistance management.

References

1) Beckerman, J. 2008. Understanding fungicide mobility. Purdue Extension BP-70-W.
2) Lyr, H. 1995. Modern selective fungicides: properties, applications, mechanisms of action. Jena, New York; Gustav Fischer, Deerfield Beach, Fla.; 595 p.
3) Fungicide Resistance Action Committee (http://www.frac.info/frac/index.htm).

Issued in furtherance of Cooperative Extension work, acts of May 8 and June 30, 1914, in cooperation with the U.S. Department of Agriculture, Robert E. Whitson, Director of Cooperative Extension Service, Oklahoma State University, Stillwater, Oklahoma. This publication is printed and issued by Oklahoma State University as authorized by the Vice President, Dean, and Director of the Division of Agricultural Sciences and Natural Resources and has been prepared and distributed at a cost of 42 cents per copy. 0409 GH

EPP-7663-8

Reference 4

Footnote: 8

FUNGICIDE RESISTANCE IN CROP PATHOGENS: HOW CAN IT BE MANAGED?

2nd, revised edition

KEITH J BRENT and DEREK W HOLLOMON

CropLife INTERNATIONAL

FRAC FUNGICIDE RESISTANCE ACTION COMMITTEE

Cover:
Scanning electron micrograph of 7-day-old colony of powdery mildew (*Blumeria graminis* f.sp. *tritici*) on a wheat leaf. Insert shows a 2-day-old colony at higher magnification. Although the sensitivity of mildew populations towards certain fungicides has changed considerably over the years, implementation of resistance management strategies has helped to sustain an overall satisfactory degree of control.
(Syngenta)

FUNGICIDE RESISTANCE ACTION COMMITTEE

a Technical Sub Group of

CROPLIFE INTERNATIONAL

Avenue Louise 143, 1050 Brussels, Belgium
Telephone: + 32 2 542 04 10. Fax: +32 2 542 04 19

www.frac.info

FUNGICIDE RESISTANCE IN CROP PATHOGENS: HOW CAN IT BE MANAGED?

KEITH J BRENT

St Raphael, Norton Lane,
Chew Magna, Bristol BS18 8RX, UK

DEREK W HOLLOMON

School of Medical Sciences
Department of Biochemistry
University of Bristol, University Walk, Bristol, BS8 1TD, UK

Published by the Fungicide Resistance Action Committee 2007

FRAC Monograph No. 1 (second, revised edition)

ISBN 90-72398-07-6
Dépot Légal: D/1995/2537/1

Design and production by Newline Graphics
Reprinted 2007

CONTENTS

SUMMARY

This publication gives a broad overview of efforts world-wide to combat problems in crop protection that are caused by development of resistance to fungicides. The following major points are emphasised:

- Fungicide treatments are, and will remain, essential for maintaining healthy crops and reliable, high-quality yields. They form a key component of integrated crop management, and their effectiveness must be sustained as long as possible.
- Pathogen resistance to fungicides is widespread. The performance of many modern fungicides has been affected to some degree.
- Resistance problems could be much worse. All types of fungicide are still effective in many situations. Current countermeasures are by no means perfect, but they have proved to be necessary and beneficial.
- Resistance builds up through the survival and spread of initially rare mutants, during exposure to fungicide treatment. This development can be discrete (resulting from a single gene mutation) or gradual (considered to be polygenic). Resistance mechanisms vary, but mainly involve modification of the primary site of action of the fungicide within the fungal pathogen.
- Resistance risk for a new fungicide can be judged to some degree. High risk indicators include: single site of action in the target fungus; cross-resistance with existing fungicides; facile generation of fit, resistant mutants in the laboratory; use of repetitive or sustained treatments in practice; extensive areas of use; large populations and rapid multiplication of target pathogen; no complementary use of other types of fungicide or non-chemical control measures.
- Monitoring is vital, to determine whether resistance is the cause in cases of lack of disease control, and to check whether resistance management strategies are working. It must start early, to gain valuable base-line data before commercial use begins. Results must be interpreted carefully, to avoid misleading conclusions.

- The main resistance management strategies currently recommended are: avoid repetitive and sole use; mix or alternate with an appropriate partner fungicide; limit number and timing of treatments; avoid eradicant use; maintain recommended dose rate; integrate with non-chemical methods. Wherever feasible, several strategies should be used together. Some are still based largely on theory, and further experimental data are needed on the underlying genetic and epidemiological behaviour of resistant forms, and on effects of different strategies. Lowering dose may not be adverse in all circumstances.
- The industrial body FRAC has been remarkably effective in its essential and difficult role of coordinating strategy design and implementation between different companies that market fungicides with a shared risk of cross-resistance. Education and dissemination of information on resistance have also been valuable activities. New types of fungicide continue to appear, and receive close attention by FRAC.
- Much research and formulation of advice on fungicide resistance have been done by agrochemical companies. Public-sector scientists and advisers also have contributed greatly to resistance management, in research and practice. Their liaison with industry has been generally good, and there are opportunities for further interaction.
- The sustained supply of new and diverse types of chemical and biological disease-control agents, and their careful introduction, are seen as key anti-resistance strategies. This aspect of product development is now increasingly recognised by national and international registration authorities, many of which now require from applicants detailed information on the actual or possible occurrence of resistance, on base-line data, and on proposed monitoring activities and instructions for use.

INTRODUCTION

'A mutable and treacherous tribe' – *this apt description of the fungi was written by Albrecht von Haller in a letter to Carolus Linnaeus, ca. 1745.*

For some 35 years now the agricultural industry has faced problems arising from the development of resistance in fungal pathogens of crops, against the fungicides used to control them. Since the first cases of widespread resistance arose, agrochemical manufacturers, academic and government scientists, and crop advisers, have put a great deal of effort into analysing the phenomenon and establishing countermeasures. In 1994 the Fungicide Resistance Action Committee (FRAC), now affiliated to CropLife International, commissioned a broad review of progress world-wide in dealing with fungicide resistance, and of the outstanding difficulties that need to be overcome.

This was published as FRAC Monograph No 1 (Brent 1995). The key tenets of resistance management have not changed over the intervening years, but there have been many developments in fungicide chemistry, in the incidence of fungicide resistance, in knowledge of resistance mechanisms, and in resistance management projects. As far as possible these have been incorporated into this Second Edition. As before, this publication aims to be an informative article for all who are concerned professionally with crop disease management, including biologists, chemists, agronomists, marketing managers, registration officials, university and college teachers, and students. It is meant to be read, or at least skimmed, as a whole. It is not intended as a detailed work of reference for the specialist, although a limited number of literature citations, out of the several thousand publications on this topic, are provided for those readers with a deeper interest. Earlier reviews concerning fungicide resistance management (Dekker, 1982; Brent, 1987; Schwinn and Morton, 1990; Staub, 1991) were drawn upon freely in the original preparation of this monograph and are still of considerable value. A review paper by Kuck (2005) has provided more recent information and comment. Where appropriate the authors have endeavoured to discuss differing viewpoints, but conclusions are theirs and do not necessarily reflect the views of FRAC.

Two further FRAC Monographs (No 2, Brent and Hollomon 1998; No.3, Russell, 2003), respectively address in more detail two major components of fungicide resistance management: the assessment of risk, and the establishment of sensitivity baselines. A second, revised edition of Monograph No. 2 is available.

CHEMICAL CONTROL OF CROP DISEASE

Fungicides have been used for over 200 years to protect plants against disease attack by fungi. From small and primitive beginnings, mainly to protect cereal seeds and grape-vines, the number of crops and crop diseases treated, the range of chemicals available, the area and frequency of their use, and the effectiveness of treatments, have increased enormously, especially since the second world war.

Remarkably, two very old-established remedies, copper-based formulations and sulphur, are still used widely and effectively. Several 'middle-aged' fungicides (phthalimides, dithiocarbamates, dinitrophenols, chlorophenyls) have been used steadily for well over 40 years. A large number of more potent fungicides, of novel structure and mostly with systemic activity not found in the earlier products, were introduced in the late 1960s and 1970s. These included 2-amino-pyrimidines, benzimidazoles, carboxanilides, phosphorothiolates, morpholines, dicarboximides, phenylamides, and sterol demethylation inhibitors (DMIs). Introductions in the 1980s mainly were analogues of existing fungicides, particularly DMIs, with generally similar though sometimes improved properties. Over the past decade, however, a number of novel compounds have been introduced commercially or have reached an advanced stage of development – these include phenylpyrroles, anilinopyrimidines, quinone outside inhibitors (QoIs, including strobilurin analogues), benzamides and carboxylic acid amides

Modern spraying of fungicides in cereal fields in Europe. Use of wide spray booms and 'tram-lines' aid timely and precise application, but the continued effectiveness of the fungicides themselves is a more basic requirement. (FRAC).

The more recent fungicides are generally used in relatively small amounts, because of their more potent action against plant pathogens. However, their margins of safety to mammals and other non-target organisms are no smaller and are often greater, when compared weight-for-weight with those of the older materials.

Spraying has always been the principal method of fungicide application, and the conventional hydraulic sprayer still predominates. Reduction in spray volume, and more stable and safer formulation, are probably the most significant advances that

have been made in application technology. The frequency and timing of spraying have not changed a great deal from early recommendations, although the advent of the systemic fungicides has permitted some greater latitude in these parameters and has increased the feasibility of using disease threshold or forecast approaches. Roughly half of the crop diseases treated require treatment only once or twice per season, and the remainder require three or more (in some cases up to 20) applications. Systems of integrated crop management involving minimum necessary chemical and energy inputs, and use of complementary non-chemical protection measures wherever possible, have been widely adopted and to some extent have led to a reduction in spray number and dose in some situations.

At present some 150 different fungicidal compounds, formulated and sold in a several-fold larger number of different proprietary products, are used in world agriculture. The total value of fungicide sales to end-users is approximately 7.4 billion US dollars (source: Phillips McDougall, Industry Overview, 2005). Nearly half of the usage is in Europe, where fungal diseases cause the most economic damage to crops. Most of the recommended treatments generally provide 90% or greater control of the target disease, and give the farmer a benefit: cost ratio of at least 3:1. Some diseases, e.g. wheat bunt caused by *Tilletia* spp. or apple scab caused by *Venturia inaequalis*, require an extremely high level of control for various commercial or biological reasons. For some others, e.g. cereal powdery mildews (*Blumeria graminis*), the risks associated with somewhat lower standards of control are smaller. Some fungicides control a rather wide range of fungal diseases, whereas others have a limited spectrum of activity against one or two specific groups of plant pathogens. Although many fungicides are marketed, any one major crop disease typically is well controlled by only three or four different types of fungicide, so that any fall in effectiveness of a previously reliable fungicide through resistance development can be a very serious matter for the grower.

DEFINING FUNGICIDE RESISTANCE

A potential new fungicide is identified in laboratory and glasshouse tests on different types of fungal pathogen, and is then tested in field trials against an appropriate range

of crop diseases in different regions and countries. Only if it works uniformly well against important crop diseases in a large number of trials over several seasons is it considered for development and marketing. The pathogens it works against are deemed to be 'sensitive', and those that it does not affect or hardly affects are regarded as 'naturally' or 'inherently resistant'. This pre-existing type of resistance is of no further practical interest once it has been identified as a limitation to the range of use of the fungicide. Reasons for natural resistance are seldom investigated, although sometimes they can be deduced from mode of action studies.

The 'fungicide resistance' we are considering here is a different phenomenon, sometimes called 'acquired resistance'. Sooner or later during the years of commercial use of a fungicide, populations of the target pathogen can arise that are no longer sufficiently sensitive to be controlled adequately. They generally appear as a response to repeated use of the fungicide, or to repeated use of another fungicide which is related to it chemically and/or biochemically through a common mechanism of antifungal action. This emergence of resistant populations of target organisms, which were formerly well controlled, has been widely known for antibacterial drugs (e.g. sulphonamides, penicillin, streptomycin) and for agricultural and public health insecticides (e.g. DDT) for almost sixty years.

Some people prefer to call this phenomenon 'insensitivity' or 'tolerance'. The former term is preferred by some plant pathologists, because they believe that fungicide resistance is easily confused with host-plant resistance to certain species or pathotypes of fungi. Some agrochemical companies have also tended to use 'insensitivity', 'loss of sensitivity' or 'tolerance', because these sound less alarming than 'resistance'. On the other hand, two studies on terminology recommended that 'resistance' should be the preferred term (Anon, 1979; Delp and Dekker, 1985). Also 'resistance' has been in use for many years to describe precisely the same phenomenon in bacteriology and entomology, and it is now very widely used with reference to fungicides also.

Workers within the agrochemical industry have objected from time to time to the use of 'resistance' to describe shifts in fungicide sensitivity occurring either in non-crop situations such as the laboratory or experimental glasshouse, or in the field but to a degree which is too small to affect disease control. They recommend that 'resistance' should denote only situations where failure or diminution of crop disease control is known to have resulted from a change in sensitivity. It is true that observations of 'resistance' generated in the laboratory, and detection of rare or weakly resistant

variants in the field, have on occasions been misinterpreted by scientific authors, or by commercial competitors, as indicating actual or impending failure of a product to perform in practice, when in fact good control was still secured.

However, attempts to restrict in this way the meaning of such a broadly used term as 'resistance' are bound to fail and to create more confusion. It is better to qualify the term when necessary. 'Field resistance' (in contrast to 'laboratory resistance') has been used sometimes to denote specifically a crop disease control problem caused by resistance. However, detection of some signs of resistance in the field can still be a far cry from having a control failure. It seems preferable to use 'field resistance' to indicate merely the presence of resistant variants in field populations (at whatever frequency or severity), and 'practical resistance' to indicate consequent, observable loss of disease control, whenever such precise terminology is necessary. 'Laboratory resistance' or 'artificially induced resistance' also are useful, precise terms which are self-explanatory. Some authors have claimed to find 'field resistance' in studies where the resistant variants actually were detected only after the field samples were subjected to subsequent selection by exposure to the fungicide in the laboratory. This is a borderline case, which is hard to categorise.

OCCURRENCE OF RESISTANCE

Table 1 gives a much condensed history of the occurrence of practical fungicide resistance world-wide, and lists major fungicide groups for which resistance is well documented. Leading examples are given of the more important diseases affected, and a few key literature references are cited. Up to 1970 there were a few sporadic cases of fungicide resistance, which had occurred many years after the fungicide concerned was introduced. With the introduction of the systemic fungicides, the incidence of resistance increased greatly, and the time taken for resistance to emerge was often relatively short, sometimes within two years of first commercial introduction. Many of the fungicides introduced since the late 1960s have been seriously affected, with the notable exceptions of the amine fungicides ('morpholines'), fosetyl-aluminium, anilinopyrimidines, phenylpyrroles and some of the fungicides used to control rice blast disease (e.g. probenazole, isoprothiolane and tricyclazole), which have retained effectiveness over many years of widespread use. Some recently introduced fungicides

Table 1
Occurrence of Practical Fungicide Resistance in Crops

Date first observed (approx.)	Fungicide or fungicide class	Years of commercial use before resistance observed (approx.)	Main crop diseases and pathogens affected	Ref*
1960	Aromatic hydrocarbons	20	Citrus storage rots, *Penicillium* spp.	1
1964	Organo mercurials	40	Cereal leaf spot and stripe, *Pyrenophora* spp.	2
1969	Dodine	10	Apple scab, *Venturia inaequalis*	3
1970	Benzimidazoles	2	Many target pathogens,	4
1971	2 Amino pyrimidines	2	Cucumber and barley, powdery mildews *Sphaerotheca fuliginea & Blumeria graminis*	5
1971	Kasugamycin	6	Rice blast, *Magnaporthe grisea*	6
1976	Phosphorothiolates	9	Rice blast, *Magnaporthe grisea*	6
1977	Triphenyltins	13	Sugar beet leaf spot, *Cercospora betae*	7
1980	Phenylamides	2	Potato blight and grape downy mildew, *Phytophthora infestans & Plasmopara viticola*	8
1982	Dicarboximides	5	Grape grey mould, *Botrytis cinerea*	9
1982	Sterol Demethylation inhibitors (DMIs)	7	Cucurbit and barley powdery mildews, *S. fuliginea & Blumeria graminis*	10
1985	Carboxanilides	15	Barley loose smut, *Ustilago nuda*	11
1998	Quinone outside Inhibitors (QoIs; Strobilurins)	2	Many target diseases and pathogens	12
2002	Melanin Biosynthesis Inhibitors (Dehydratase) (MBI D)	2	Rice blast, *Magnaporthe grisea*	13

*References: 1. Eckert, 1982; 2. Noble *et al*. 1966; 3. Gilpatrick, 1982; 4. Smith, 1988; 5. Brent, 1982; 6. Kato, 1988; 7 Giannopolitis, 1978; 8 Staub, 1994; 9. Lorenz, 1988; 10. De Waard, 1994: 11. Locke, 1986; 12. Heaney *et al*. 2000; 13. Kaku *et al*. 2003.

such as benzamides and carboxylic acid amides have not yet encountered serious resistance problems, possibly because of the management precautions which have been taken. Most of the older materials such as copper fungicides, sulphur, dithiocarbamates (e.g. mancozeb), phthalimides (e.g. captan) and chlorothalonil, have retained their full effectiveness in all their uses, despite their extensive and sometimes exclusive use over many years.

Often the onset of resistance has been associated with total, or almost total, failure of disease control. Indeed it was growers' observations of obvious and sudden loss of effect that generally gave the first indication of resistance. Of course it was necessary to show that resistance really was the cause, by checking for abnormally low sensitivity of the pathogen in tests under controlled conditions. There was, and to some extent still is, a temptation for growers and advisers to blame resistance for all cases of difficulty of disease control. There are many other possible reasons, such as poor application, deteriorated product, misidentification of the pathogen, unusually heavy disease pressure. However, there remained many examples where no other explanation was found, and where serious loss of control was clearly correlated with greatly decreased sensitivity of the pathogen population as revealed in laboratory tests on representative samples.

Resistance of the kind just described, characterised by a sudden and marked loss of effectiveness, and by the presence of clearcut sensitive and resistant pathogen populations with widely differing responses, is variously referred to as 'qualitative', 'single-step', 'discrete', 'disruptive' or 'discontinuous' resistance (Fig.1). Once developed, it tends to be stable. If the fungicide concerned is withdrawn or used much less, pathogen populations can remain resistant for many years; a well-documented example is the sustained resistance of *Cercospora betae*, the cause of sugar-beet leafspot, to benzimidazole fungicides in Greece (Dovas *et al*., 1976). A gradual recovery of sensitivity can sometimes occur, as in the resistance of *Phytophthora infestans*, the potato late blight pathogen, to phenylamide fungicides (Cooke *et al*., 2006). In such cases, resistance tends to return quickly if unrestricted use of the fungicide is resumed, but re-entry involving also a partner fungicide has proved useful in some instances.

Sometimes, as in the case of the DMI fungicides, and of the 2-amino-pyrimidine fungicide ethirimol, resistance has developed less suddenly. In such cases, both a decline in disease control and a decrease in sensitivity of pathogen populations as

revealed by monitoring tests, manifest themselves gradually, and are partial and variable in degree. This type of resistance is referred to as 'quantitative', 'multi-step', 'continuous', 'directional' or 'progressive' (Fig.1). It reverts rapidly to a more sensitive condition under circumstances where the fungicide concerned becomes less intensively used and alternative fungicides are applied against the same disease.

The first appearance of resistance in a particular fungicide-pathogen combination in one region has almost always been accompanied, or soon followed, by parallel behaviour in other regions where the fungicide is applied at a similar intensity. Whether the fungicide also meets resistance in other of its target pathogens depends on the individual case. Generally it does occur in other target pathogens that have a comparable rate of multiplication, provided that the fungicide is used in an equally

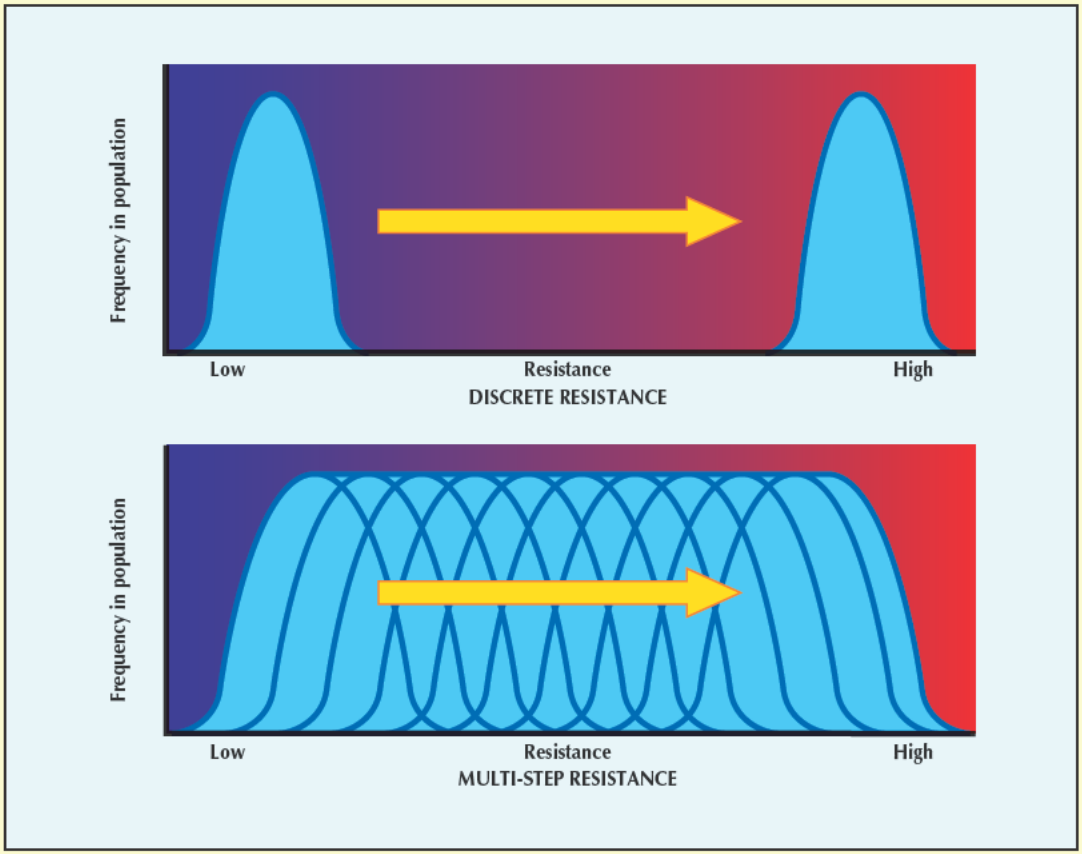


Fig. 1
Diagrams showing the bimodal and unimodal distributions of degree of sensitivity which are characteristic of the discrete and multi-step patterns of resistance development. Blue shading indicates original sensitive population, and red shading subsequent resistant population.

intensive way. It is notable that rust fungi, despite their abundant sporulation and rapid spread, appear to be low-risk, seldom producing resistance problems (Grasso *et al*., 2006).

Pathogen populations that develop resistance to one fungicide automatically and simultaneously become resistant to those other fungicides that are affected by the same gene mutation and the same resistance mechanism. Generally these have proved to be fungicides that bear an obvious chemical relationship to the first fungicide, or which have a similar mechanism of fungitoxicity. This is the phenomenon known as 'cross-resistance'. For example, pathogen strains that resist benomyl are almost always highly resistant to other benzimidazole fungicides such as carbendazim, thiophanate-methyl or thiabendazole. Sometimes cross-resistance is partial, even when allowance is made for the greater inherent activity of different members of a fungicide group.

There is a converse phenomenon, 'negative cross-resistance', in which a change to resistance to one fungicide automatically confers a change to sensitivity to another. This is much rarer, but several cases are well characterised; one, involving carbendazim and diethofencarb, has been of practical importance and is discussed later.

Some pathogen strains are found to have developed separate mechanisms of resistance to two or more unrelated fungicides. These arise from independent mutations that are selected by exposure to each of the fungicides concerned. This phenomenon is totally different from cross-resistance in its origin and mechanism, and is usually termed 'multiple resistance'. An example is the common occurrence of strains of *Botrytis cinerea* that have become resistant to both benzimidazole and dicarboximide fungicides.

ORIGINS OF RESISTANCE

Once it arises, resistance is heritable. It results from one or more changes in the genetic constitution of the pathogen population. There is overwhelming circumstantial evidence that a mutant gene that causes production of a particular resistance mechanism pre-exists in minute amounts in the population. Before the fungicide was

ever used in the field, such a mutation would confer no advantage to the growth or survival of the organism, and could well cause a slight disadvantage. Hence it would remain at a very low frequency, probably dying out and re-appearing spontaneously many times.

Spontaneous mutations of all kinds are continually occurring in all living organisms. The rate of mutation can be increased greatly in the laboratory by exposing the organism to ultra-violet light or chemical mutagenic agents, and thus resistant mutants can be produced artificially. However, it cannot be assumed that such artificial mutants are necessarily identical in resistance mechanism or in other respects to those that arise in the field.

Typically, a resistant mutant might exist at an initial frequency of the order of 1 in 1000 million spores or other propagules of the pathogen. Amongst the survivors of a fungicide treatment, however, the resistant forms will be in much higher proportion ('the survival of the fittest'). It is only when this reaches say 1 in 100 or even 1 in 10 in the population that difficulty of disease control and the presence of resistant individuals will have become readily detectable. Thus the obvious onset of resistance is often sudden, but prior to this the resistance will have been building up insidiously at undetectable levels. If a fungicide treatment is very effective, with few survivors, selection will be very rapid. If the fungicide is only 80% effective, then after each treatment the number of variants will be concentrated only 5-fold and the build-up will be slower.

Several fairly obvious but important deductions, which can influence assessment of risk and design of avoidance strategies, can be made from consideration of this simple process of mutation and selection. Accumulation of resistant mutants will be enhanced by higher frequency of treatment with the fungicide concerned, by a more effective application method or dose, by the presence of larger pathogen populations before treatment, and by greater spore production and shorter generation times in the pathogen.

The selection process outlined above is based on much genetic analysis of sensitive and resistant strains, and on much field experience. However, it represents the simplest form of resistance, the discrete pattern referred to earlier, which is also termed 'major gene' resistance. One point mutation causing a single amino acid change in the target protein is responsible for a high level of resistance, and the sensitive and resistant forms fall into very distinct classes. This pattern is characteristic of resistance to

several major groups of fungicides including benzimidazoles, phenylamides, dicarboximides and QoIs. Other mutations in the target protein may give rise to lower levels of resistance. For example, the F129L mutation in the b-cytochrome target of QoIs causes only low levels of resistance in many pathogens, and hence is of little practical importance, in contrast to the G143A mutation which causes a high degree of resistance, and consequent loss of disease control (Gisi *et al*. 2002).

A somewhat different 'polygenic' process of genetic change is thought to underlie the 'quantitative' or 'multi-step' pattern of resistance. Again resistance results from the selection of mutants, but in this case a number of different genes, each with a partial effect, appear to be involved. The more genes that mutate to resistance-causing forms, the greater the degree of resistance. This would account for the gradual observable development of resistance, and for the continuous range of sensitivity that can be found (Fig.1). Although the theory of polygenic resistance is widely accepted, it must be said that the genetic evidence for polygenic resistance in field isolates is rather thin. The best known and most studied examples of continuous resistance in practice have been in cereal powdery mildews, which are rather hard to study genetically, and some of the data are conflicting (Hollomon, 1981; Hollomon *et al*., 1984; Brown *et al*., 1992). Biochemical evidence for polygenic resistance to azole (DMI) fungicides indicates involvement of at least four resistance mechanisms which are discussed below. However, Sanglard *et al*. (1998) studying the human pathogen *Candida albicans*, found that different mutations in the same target-site gene may accumulate in a single strain, and their individual effects may be additive, or possibly synergistic. In this way polyallelic changes may contribute to multistep development of resistance.

QoIs (strobilurins) are the first fungicide class to target a protein (cytochrome bc-1) that is encoded by a mitochondrial gene. DNA repair mechanisms are less effective for mitochondrial DNA than for nuclear DNA, and consequently mitochondrially encoded genes are more liable to mutation. The frequency of DNA base changes in mitochondrial DNA is further increased by its close proximity to reactive oxygen species generated during respiration. Depending on the impact of these mutations on fitness, resistance seems likely to develop quickly where target sites are encoded by mitochondrial genes. Onset of resistance to QoIs was in fact rapid in a number of pathogens, although it must be noted that benzimidazole resistance, resulting from a nuclear mutation, developed equally quickly.

RESISTANCE MECHANISMS

Sampling barley powdery mildew (*Blumeria graminis*). Leaves bearing pustules are removed with scissors, and the spores are used as inoculum for sensitivity tests in the laboratory.
(Bayer CropScience)

Collecting samples of *Botrytis cinerea* from grapes by a battery-driven, portable spore-trapping device. A vacuum deposits spores on a fungicide containing agar plate.
(M.L.Gullino, University of Turin)

A large amount of experimental effort has focussed on this subject, particularly in academic laboratories. A broad outline of current information is given in Table 2. Some of the information is derived from resistant strains generated in the laboratory (e.g. for quinoxyfen) and not from field isolates. We now understand well the most important mechanisms of resistance to the benzimidazole, carboxanilide, phosphorothiolate, dicarboximide, and QoI fungicides. There is extensive information concerning the DMI fungicides, identifying four major resistance mechanisms that may operate. However, there are still many gaps in our knowledge, not only for established fungicide groups (e.g. anilinopyrimidines), but also for new fungicide groups defined by cross-resistance (e.g. carboxylic acid amides, CAAs).

Many types of resistance mechanism are known. These include: alteration of the biochemical target site so that it is no longer sensitive; increased production of the target protein; developing an alternative metabolic pathway that bypasses the target site; metabolic breakdown of the fungicide; exclusion or expulsion of the fungicide through ATP-ase dependent transporter proteins.

By far the commonest mechanism appears to be an alteration to the biochemical target site of the fungicide. This could explain why many of the older products have not encountered resistance problems. Once they have penetrated the fungal cell, the older fungicides act as general enzyme inhibitors, affecting many target sites (hence they are sometimes called 'multi-site' inhibitors). They act selectively on fungi, rather than on plants and animals, because they penetrate and accumulate much more readily in fungi. Many sites in the fungus would have to change simultaneously in order to stop the fungicide from working. The chances of the many necessary genetic changes happening are negligible, and in any case an organism with so many alterations would be highly unlikely to be pathogenic or even viable. The occasional cases of resistance to multi-site fungicides presumably have resulted from other types of mechanism, not involving the sites of action.

In contrast, modern fungicides act primarily at single target sites, and are often referred to as 'single-site' or 'site-specific' fungicides. Thus just a single gene mutation can cause the target site to alter, so as to become much less vulnerable to the fungicide. The rapid development over the past 10 years of PCR-based diagnostic methods for

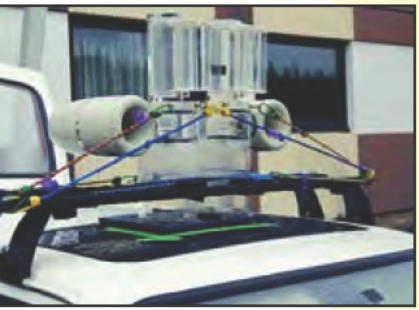
Table 2
Mechanisms of Fungicide Resistance

Fungicide or fungicide class	Mechanism of resistance
Aromatic hydrocarbons	Unknown, but show cross-resistance with dicarboximides and phenylpyrroles
Organo-mercurials	*Detoxification by binding substances
Dodine	Unknown
Benzimidazoles	Altered target site (ß-tubulin)
2-Amino-pyrimidines	Unknown
Kasugamycin	Altered target site (ribosomes)
Phosphorothiolates	Metabolic detoxification
Phenylamides	Possibly altered target site (RNA polymerase)
Dicarboximides and Phenylpyrroles	*Altered target site (protein kinase involved in osmoregulation)
DMIs	Increased efflux; altered target site; decreased demand for target-site product; target-site over-production
Carboxanilides	Altered target site (succinate-ubiquinone oxidoreductase)
QoIs (strobilurins)	Altered target site (ubiquinol-cytochrome c reductase)
Melanin Biosynthesis Inhibitors (Dehydratase) MBI-D	Altered target site (scytalone dehydratase)

*Some doubt regarding occurrence in field isolates

Reviews by Leroux *et al.*, 2002; Yamaguchi and Fujimura, 2005; Brent and Hollomon, 2007; provide further information

detection of point mutations causing resistance has aided the identification of resistance mechanisms, especially those involving target site changes. Several major resistance genes have now been isolated and characterised. In each case a single point mutation causes a change in a single amino acid in the target protein so that the fungicide no longer binds so tightly. Different amino acid changes in a target protein can cause different levels of resistance. For instance, as mentioned earlier, the G143A mutation (causing glycine to be replaced by alanine) at amino acid position 143 in the b-cytochrome of mitochondrial Complex III, causes higher levels of resistance to QoIs



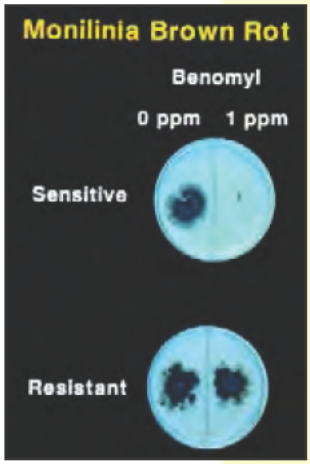
Wind impaction spore trap, mounted on a car roof. This has been used to test for shifts in sensitivity of aerial cereal powdery mildew spores. The trap contains fungicide-treated leaf pieces
(Syngenta)

than the less common F129L mutation (replacing phenylalanine by leucine at position 129) (Sierotzki *et al.*, 2005).

The way in which polygenic systems operate to give different degrees of resistance are less clearly understood. The relatively low level of resistance caused by each gene makes the mechanisms of resistance particularly hard to determine. In the case of the DMI fungicides there is some evidence that mutation of different genes may elicit a number of different resistance mechanisms listed in Table 2 (De Waard *et al.*, 2006). These are unrelated, but can act simultaneously and possibly in a synergistic way.

It is interesting that those few fungicides that are not directly fungitoxic, but which act indirectly by affecting defence mechanisms in the host plant, e.g. probenazole, have not encountered resistance. Reasons for this are not clear.

MONITORING: OBTAINING THE FACTS



Radial-growth test on two strains of *Monilinia fructicola* (stone fruit brown rot pathogen) on split agar plates.
(Du Pont)

By 'monitoring for fungicide resistance' we mean testing samples of field populations of target pathogens for their degree of sensitivity to one or more fungicides. This is a crucial area of resistance research, because virtually all our knowledge of the distribution, evolution and impact of resistance in the field has depended on monitoring. It was originally done in the early 1960s to investigate possible resistance in seed-borne diseases of wheat and oats, and in storage mould on citrus fruit. A much larger amount of monitoring is now routinely done world-wide.

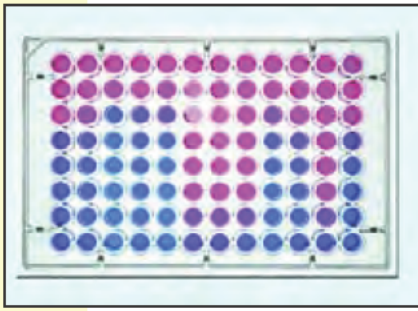
Monitoring can be done to gain early warning of an impending resistance situation. However, as discussed above, single-step resistance only becomes readily detectable in field samples when a relatively high frequency of the resistant variants (>1%) is reached. The next or next-but-one treatment would fail to give normal control. Therefore useful early warning is unlikely to be obtained, unless impractically large numbers of samples are tested (300 samples are needed to give a 95% chance of detecting resistance at 1% frequency).With multi-step resistance, partially resistant strains can exist at high frequency before practical loss of disease control occurs. Detection of these is feasible, so that in this case monitoring can indicate the risk of more severe resistance developing and causing loss of control. If a molecular method has been developed (see below) because a resistance problem has emerged elsewhere,

and the mechanism involved identified, detection of a single step mutation can be achieved at much lower frequencies, allowing earlier warning of the need to implement anti-resistance strategies.

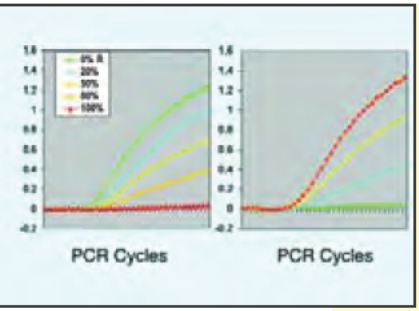
Another important reason for monitoring is to check that management strategies are working. This involves monitoring regularly over large areas of use, an expensive operation but one which has been justified by situations of high commercial risk. Molecular diagnostics have been successfully used to monitor the degree of success of anti-resistance strategies aimed at combating QoI resistance in powdery mildew and septoria diseases of wheat (Fraaije *et al*., 2002; 2005). Monitoring is also done at specific sites in order to investigate complaints from growers of an apparent loss of performance of the fungicide, and/or to give guidance on the selection of future fungicide treatments at the site or in the district.

Many otherwise competent monitoring operations have, in the past, given inconclusive results because one or both of two extremely important steps have been omitted. The first of these is to develop monitoring methods early, and then to use them to obtain base-line data on typical pathogen populations before they are exposed to any widespread use of a new fungicide. This initial assessment of the 'natural' range of sensitivity, which can be considerable, is an enormous help to the interpretation of any later monitoring data in terms of possible shifts in sensitivity. It also ensures that suitable sampling and assay methods have been worked out and tested. Unfortunately, until recent years base-line data were all too rarely obtained. However, largely because of registration requirements, the agrochemical industry is now committing the resources needed to obtain such data prior to commercialisation. FRAC Monograph No. 3 *Sensitivity Baselines in Fungicide Resistance Research and Management* (Russell, 2003) gives a full account of the rationale and methodology of baseline construction.

A second crucial activity to complement resistance monitoring, is to monitor practical performance. Knowledge of the continued degree of effectiveness of field performance is often surprisingly vague and badly recorded, and yet it is a critical indicator of the occurrence of practical resistance. Systematic observations, year by year, must be made on amounts of disease in commercial crops treated and untreated with the at-risk fungicide, and also in any replicated plot trials that are done. In order to confirm that practical resistance has appeared, it is essential to establish a clear correlation, both in time and geographically, between the incidence of resistant



High throughput micro-titre plate assay for sensitivity to azoxystrobin in *Mycosphaerella graminicola*. Twelve isolates were each tested against eight different azoxystrobin concentrations, in the presence of the growth indicator dye, Alamar Blue which turns red where pathogen growth occurs. This test shows four azoxystrobin-resistant isolates.
(B A Fraaije, Rothamsted Research)



Real-time PCR detection of the G143A mutation causing resistance to QoI fungicides. Different labelled probes or primers are used to identify sensitive (left) or resistant (right) alleles. Tests can be formatted to allow the determination of the frequency of resistant alleles in a population.
(B A Fraaije, Rothamsted Research)

biotypes and the deterioration of field performance of the fungicide. Evidence for the latter should be recorded and collated, and not merely anecdotal.

Much experience has now been gained with regard to the reliability, logistics, costs and necessity of monitoring. Timely and representative sampling is vital. It has been found very revealing to obtain some samples of the pathogen early in the season before treatment starts, if sufficient infection exists. The observation of a high resistance level after treatment can actually be a sign of very successful control, the resistant forms being concentrated in the small surviving population. Of course practical problems would follow if the resistant population persisted and formed the inoculum for the following year, but this is not necessarily the case. Experience has also shown that the risk of resistance can vary greatly between regions where disease pressures and fungicide use are high, and neighbouring areas where there is less disease or where yields are too low to support widespread fungicide use. For example, in Northern Europe several key cereal pathogens have developed resistance to a

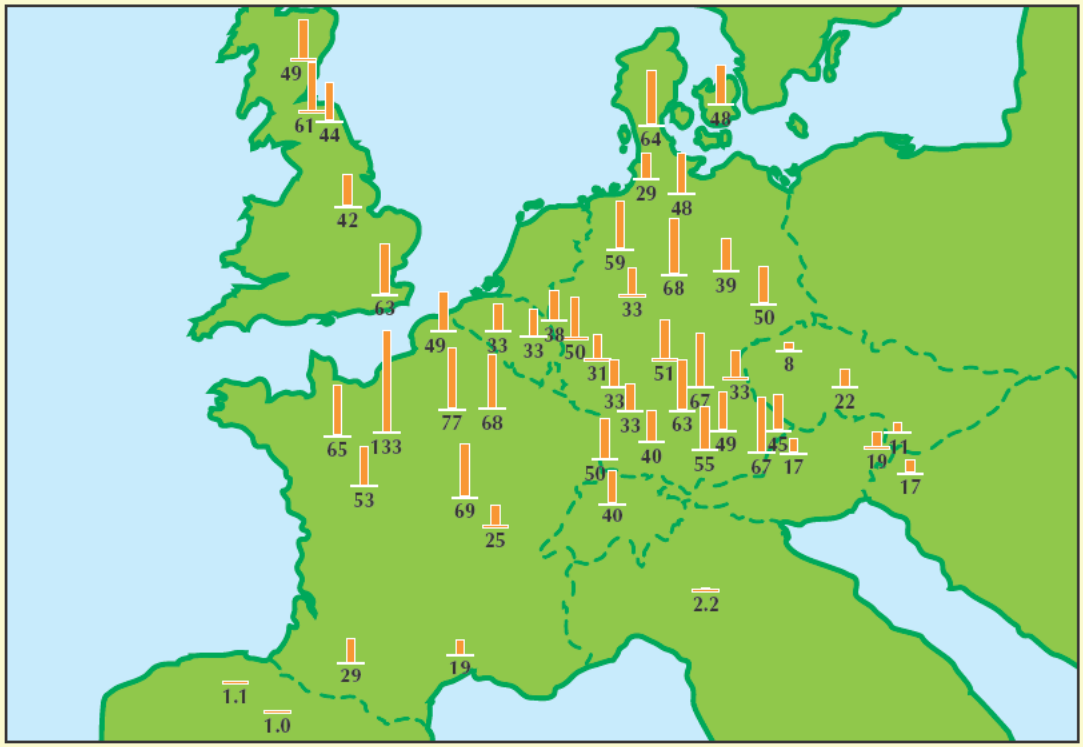


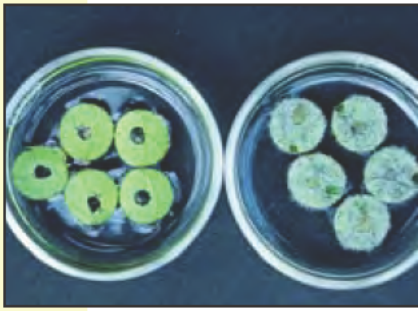
Fig. 2
Results of a large-scale monitoring programme for resistance of wheat powdery mildew to triadimenol across Europe. Values are 'resistance factors' for 1993 (or 1992 for Spain), i.e. ratios of the fungicide concentrations required to give 50% inhibition of a field sample and of a standard wild-type strain). Large regional differences were found, with resistance greatest in the north-west where DMI fungicide use had been most intense.
(From Felsenstein, 1994)

number of fungicide groups, whereas in southern Europe the same pathogens have remained sensitive, and the requirement for monitoring is less important (Kuck, 2005).

Sensitivity testing methods must be able to give realistic, quantitative, reproducible and readily understandable results. Standardisation of methods has been an aim of a number of organisations, including EPPO and FRAC. Details of recommended methods were published up to 1992 (Anon, 1991; Anon, 1992), and FRAC is now planning to publish a catalogue of new methods on its webpage at www.frac.info. Standardisation does enable direct comparisons to be made between results obtained by different research centres, especially if an isolate of known sensitivity is tested at each centre. On the other hand, pressure to conform must be applied with caution. If a diversity of methods give similar results, as is generally the case, this actually strengthens confidence in the results. Also it is often hard to judge the advantages and problems of different methods until several years' experience of their use have been gained. Different situations may be best suited by the use of different or modified tests. A few examples of the wide range of methods that have been used are shown in the photographs.

The cornerstone of monitoring remains some form of bioassay, so that a decrease in sensitivity is identified regardless of the underlying mechanism. In recent years tests have been miniaturised where possible. Spore germination assays are done in various multi-well plate formats, permitting larger numbers of samples to be tested. Growth in a liquid medium can be measured for some fungi directly in a spectrophotometer, or by measuring respiration using reduction of a fluorophore (e.g. 4-methylumbelliferyl-N-acetyl-ß-D- glucosaminide) as an indicator (Fraaije *et al*., 2005). But bioassays can be very resource-demanding, especially when applied to obligate parasites such as downy and powdery mildews. Where molecular mechanisms of resistance are known, and point mutations causing them defined, various PCR technologies can be applied to detect Single Nucleotide Polymorphisms (SNPs, McCartney *et al*., 2003; Fraaije *et al*., 2005). The early recognition of the correlation between a single amino acid change (G143A) in the QoI target b-type cytochrome, provided the impetus for large-scale, high-throughput monitoring of QoI resistance using allele-specific real-time PCR (Collina *et al*., 2005; Kianianmomemi *et al*., 2007). Indeed, current monitoring for QoI resistance is almost entirely dependent on real-time PCR diagnostic technologies, which have proved capable of detecting point mutations at frequencies within field populations as low as 1 in 10^8 .

Whole plant test on sensitive strain of apple powdery mildew (*Podosphaera leucotricha*). Plants untreated (left) or sprayed with 100ppm benzimidazole (right).
(From Anon, 1991)
(DuPont)



Potato leaf disc test on *Phytophthora infestans* (late blight pathogen) with sensitive (left) and resistant (right) spore inocula. Discs are floating on 1 ppm metalaxyl solution.
(Syngenta)

When a point mutation causing resistance is identified in one pathogen, the corresponding sequence can be determined in another pathogen, and a PCR diagnostic assay developed even before practical resistance has been identified in that pathogen (Windass *et al*., 2000). So far, PCR-based monitoring in this way has been restricted to QoI resistance in a large number of pathogens, although application of PCR technology to monitor resistance in other pathogen/fungicide combinations where point mutations causing resistance are well known (e.g. resistance to benzimidazoles, dicarboximides and carpropamid) would be technically feasible.

Interpretation of monitoring results has proved difficult in the past and at times it has resulted in misleading over-prediction of resistance problems. There has been exaggeration of the practical significance of slight variation in sensitivity between field samples, or in the detection of resistant biotypes at low frequency or after a period of artificial selection. This has partly arisen from a lack of rigorous reporting and discussion of results in detailed scientific papers, in favour of verbal reports or brief meeting abstracts. In general, however, careful monitoring, linked to good base-line data and close observation of field performance, has yielded much information of scientific and practical value, and will continue to do so.

Large-scale international programmes of monitoring for insecticide resistance have been organised by FAO and WHO (cited in Brent, 1986). Comparable programmes have not been conducted for fungicides, and it is questionable whether such large schemes are appropriate. To date, the most extensive monitoring programmes for fungicide resistance have been Europe-wide surveys over a number of years of several cereal and grape diseases. Funded by contracts with the agrochemical industry, these surveys were initially carried out by workers at the Technical University of Munich, Fig 2, and more recently by companies specialising in this type of work, such as Epilogic, Biotransfer and Biorizon. More limited surveys within a country may be funded mainly by agrochemical companies or grower organisations, and done either by the agrochemical companies themselves, or by public sector or private research organisations.

ASSESSING THE RISK

This is a matter of great importance to the chemical manufacturer who is about to develop a new product. Knowledge of the risk of resistance will help to determine whether the product should be developed and marketed, and, if so, of what nature and how stringent should be the resistance management strategies and how much further monitoring should be done.

The possibility that strains resistant to existing fungicides may be cross-resistant to the candidate product is readily determined. The chemical structure of the potential product, or its mode of action if known, may resemble those of existing fungicides, and thus indicate a likelihood of cross-resistance. More direct guidance can be obtained by testing the candidate against field isolates of the target pathogen that are known to resist other fungicides, and this is now done as a matter of routine. If cross-resistance is not found in laboratory tests, and if the field trials are uniformly successful, there still remains the risk of selection and build-up of initially rare resistant mutants during commercial use. This risk is impossible to assess with any precision, but some clues can be obtained, which permit a rough but useful estimation of risk at low, moderate or severe levels. FRAC Monograph No. 2 *Fungicide Resistance: The Assessment of Risk* (2nd revised edition, Brent and Hollomon, 2007) addresses this topic in more detail.

Knowledge of the mechanism of action of a fungicide can be informative. For example, a mechanism involving inhibition of tubulin assembly would, by analogy with the benzimidazole fungicides, be considered a high risk indicator, whereas a multi-site action would indicate relatively low risk.

The potential for mutation to resistance is best studied by treating target fungi with mutagenic chemicals or ultra-violet light, exposing the treated cultures to the new fungicide, and isolating and testing the survivors for resistance. It has long been considered that failure to generate resistant mutants, with unimpaired fitness, in the laboratory may indicate stability of performance in the field, as for example with multi-site fungicides (Georgopoulos, 1994). Conversely the ready production of such mutants could indicate a potential for practical resistance problems, as shown with benzimidazoles, phenylamides and QoIs.

However, ease of mutant production has certainly not proved to be a totally reliable indicator. Mutants that resist the amine (morpholine) fungicides are easy to obtain in the laboratory, but serious practical resistance problems have still not occurred over the many years of extensive use of these fungicides. Mutants of several fungi which were resistant to DMI fungicides were readily obtained in the laboratory, but these had reduced growth rate and sporulation and their degree of resistance was inversely proportional to pathogenicity. In view of these indications of decreased fitness in the field it was concluded that practical resistance would be unlikely (Fuchs and Drandarevski, 1976). Subsequently such resistance in fact appeared, although relatively slowly. In a risk evaluation study on the phenylpyrrole fungicide fludioxonil, resistant strains of *Botrytis cinerea* were obtained in the laboratory, and found to be cross-resistant to dicarboximides. However, dicarboximide-resistant field isolates proved to be sensitive to fludioxonil, and the latter did not select for dicarboximide resistance in field experiments (Hilber *et al*., 1994).

Thus the reliability of genetic experimentation in predicting resistance risk is still a matter of debate, although the consensus view is probably that it gives useful indications for consideration along with other evidence. The degree of correlation between the ease of production of resistant mutants in mutagenic and crossing experiments, their fitness and pathogenicity, and the subsequent occurrence of field and practical resistance, is an important and interesting topic which deserves more research.

Repeated exposure of successive generations of a pathogen to sub-lethal concentrations of a fungicide, sometimes called 'training' or forced selection, might be expected to indicate practical resistance risk. This approach was used to study potential resistance of *Phytophthora infestans* to phenylamides. Resistant strains could be selected *in vitro*, but these either were not pathogenic or could not infect phenylamide-treated plants. Selection on potato plants for 11 generations did not yield any resistant strains (Staub *et al*., 1979). In contrast, exposure of a related fungus to a mutagenic chemical (a nitrosoguanidine) yielded many highly phenylamide-resistant, virulent strains which could infect treated plants (Davidse, 1981). These different outcomes suggested that physically or chemically induced mutagenesis may be more revealing than 'training' in resistance risk studies. Probably this is because starting populations in the laboratory are too small to include the range of spontaneous mutants that occur in field populations. When mutagens are used it is important that

precautions are taken to avoid the risk of releasing resistant strains into host crops in the locality. More research studies comparing mutagenesis and 'training' as predictors are warranted, in relation both to discrete and multi-step resistance development in practice.

The potential for selection of resistant mutants has from time to time been studied in field-plot experiments in which a fungicide is applied repeatedly under conditions which favour infection by a target pathogen. However there seem to be no recorded instances of where such experimentation has yielded useful predictions of either future field problems or their absence. If intensive treatments in the field do generate for the first time fit, resistant pathogen strains then there is a danger that they could spread and initiate problems of control, and suitable precautions must be taken.

As discussed earlier, classes of fungicide differ greatly in their basic vulnerability to resistance arising in target pathogens. Indications of the degree of this intrinsic fungicide risk, whether low, medium or high level, can emerge from mutagen treatments or training experiments, or more reliably (although only after first commercial introduction) from performance-checking and monitoring during early years of commercial use, and from cross-resistance studies.

Different classes of pathogen also vary in their ability to become resistant to fungicides. A number of biological factors are involved in pathogen risk, and can be considered to act together in an additive way (Gisi and Staehle-Csech, 1988a, b; Brent *et al*., 1990). Higher pathogen risk is associated with a shorter life cycle, more abundant sporulation of the pathogen, and rapid, long-distance dispersal of spores. For example, resistance to the benzimidazole fungicides was much slower to develop in cereal eyespot disease, where the pathogen (*Oculimacula* spp.) generally has only one generation per year, with limited spore production and dispersal, and only one fungicide application is made per year, than in cucurbit powdery mildew (*Sphaerotheca fuliginea*) which has many short generations, abundant sporulation and widespread dispersal, and requires repeated fungicide treatments. There are some factors underlying the degree of pathogen risk, probably involving pathogen-specific genomic behaviour, which are not fully understood. For example, it is not clear why rust fungi, despite abundant sporulation and short generation times, have caused no major problems of fungicide resistance. The way in which 'fungicide risk' and 'pathogen risk' combine to determine the overall intrinsic risk of resistance problems is illustrated in Fig. 3.

Fig. 3
Matrix diagram to exemplify how separate and sometimes differing degrees of resistance risk are associated with the use of a particular fungicide class, and with the control of a particular target pathogen. Estimates are approximate and based on experience to date. Blue shading indicates lower risk, and red shading higher risk.

Overall risks of resistance development in crop disease situations depend not only on these intrinsic or inherent risks attached to particular types of fungicide or pathogen, but also on the conditions of fungicide use. Unlike the intrinsic risks, the conditions of use can vary much between regions and from farm to farm. They comprise environmental factors, especially climatic and topographic conditions that affect the severity and spread of crop disease, and a range of farmer-determined agronomic factors. The latter include fungicide selection, application frequency and dose, use of glass-houses or polythene tunnels (these tend to isolate pathogen populations and prevent ingress of sensitive strains), pattern of crop rotation, choice of cultivar and its degree of susceptibility to infection, and the extent of use of hygienic practices. If the regional environment and farm practices tend not to favour disease development and

spread, and hence reduce the need for intensive fungicide use, and if the exclusive use of the at-risk fungicide is restricted or avoided, then the overall risk of resistance problems will be smaller.

Assessment of degree of risk of resistance development for a particular location must take into account and integrate as far as possible all influential factors including the intrinsic risk for each fungicide-pathogen combination, the environmental conditions and their likely effects on disease incidence, and relevant agronomic practices which should incorporate any specific fungicide use strategies recommended by the fungicide manufacturer. Inevitably, such risk assessment can only be an approximate estimate, at best indicating low, medium or high level, because many factors are involved, and with our present state of knowledge their effects cannot be measured precisely or given accurate weightings for relative importance.

MANAGEMENT STRATEGIES

Theoretical argument, experimental evidence and practical experience all indicate that the build-up of resistance is greatly favoured by the sustained, sole use of fungicides with specific mechanisms of action. Conversely, their occasional use, interspersed by the use of other, unrelated products is unlikely to lead to resistance problems. In practice, however, resistance management strategies must combine the long-term conservation of fungicide effectiveness with an amount and pattern of use that are sufficient both to satisfy the needs of the farmer and to provide a reasonable pay-back to the manufacturer. It is not an easy task to design and implement such well-balanced programmes.

Strategies must be applied uniformly over large areas in order to obtain their full biological benefit, and also to ensure that any short-term commercial disadvantage and long-term advantage are shared amongst all manufacturers of the same group of fungicides. Thus to have a chance of success any strategy must be reached by agreement and depend upon a commitment to implementation from all supply companies involved. It must also be understandable and acceptable to the farmer. To achieve all this, on the basis of limited data and understanding of the phenomenon, is the difficult but important major aim of FRAC.

The approaches taken for different groups of fungicides will be discussed later, but first let us consider briefly the range of use strategies for resistance management that are available. Although they are discussed individually, the integrated use of combinations of different strategies is feasible, beneficial, and often implemented.

1. Do not use the product exclusively

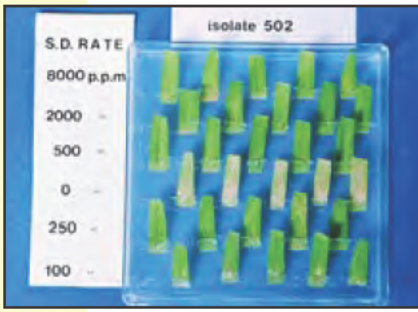
Apply it as a mixture with one or more fungicides of a different type, or as one component in a rotation or alternation of different fungicide treatments.

The 'companion' or 'partner' compounds applied in either of these ways will dilute the selection pressure exerted by the at-risk fungicide and inhibit the growth of any resistant biotypes that arise. The companion compound can be a multi-site compound known to have a low risk of inducing resistance. Alternatively, it can be a single-site fungicide that is known not to be related to its partner by cross-resistance or (in the absence of known resistance) by a similar mode of action. Use of a mixture of two single-site fungicides must carry some element of risk of selecting dual-resistant strains. However, the chances of two mutations occurring simultaneously will be very small compared to that of a single mutation (e.g. 10^{18} instead of 10^{9}). Consecutive development of double resistance could occur, but would seem much less likely to develop than if the two components were used separately and repeatedly.

This type of strategy is widely recommended by industry and also by advisory bodies. The use of formulated ('pre-packed') mixtures of two different fungicides has often been favoured by manufacturers. If an at-risk fungicide is not sold alone, then use of the mixture is the only use option open to the farmer and implementation of the strategy is ensured. Also the control of many pathogens only requires one or two treatments per annum so that the rotational approach is not appropriate. Mixtures are of course also marketed for other purposes, such as broadening the range of pathogens which can be controlled or enhancing control by increasing the duration of protection. Questions of what application rate is appropriate for each mixture component are difficult and have been debated many times. Some reduction relative to the full recommended separate rates has often been made, to keep down costs. This may reduce selection pressure for the 'at risk' fungicide, but clearly it is vitally important to maintain the companion compound at a level where it can still exert an effective independent action against the target pathogens

Numerous mathematical models predicting rate of development of resistance in relation to different regimes of fungicide use have been published, and are discussed

by Brent *et al.* (1990), Birch and Shaw (1997), and Brent and Hollomon (2007). They reveal that two basic principles underlying resistance management are to reduce the growth rates of both sensitive and resistant types, and to reduce the growth rate of the resistant type relative to the sensitive type (Fry and Milgroom, 1990). Most of the strategies that are used involve one or both of these effects. The models all indicate that use of both mixtures and rotations can delay, but not prevent, the build-up of resistant variants. They favour one or other of these two approaches to different degrees depending on the various assumptions that are incorporated. Experimental data relating to the effectiveness of mixture and rotation strategies are limited. Growth-room and plastic-tunnel studies on *Phytophthora infestans*, showed that applications of mixtures of a phenylamide fungicide with mancozeb or mancozeb plus cymoxanil decreased the build-up of phenylamide resistance, compared with phenylamide alone (Staub and Sozzi, 1984; Samoucha and Gisi, 1987). Selection for QoI resistance in *Plasmopara viticola* was delayed by a mixture with folpet, fosetyl-aluminium or mancozeb (Genet *et al.*, 2006). Whilst small-scale studies such as these, done under controlled conditions and with prepared inocula, can give clear and reproducible results, there is also a need to test strategies against the much larger and more diverse populations that occur in the field.



Leaf segment test on barley powdery mildew. Spores from one field isolate are dusted on segments from plants grown from seed treated with different ethirimol concentrations. (Syngenta).

A recent modelling study (Parnell *et al.*, 2006) has predicted that the regional spread of single gene resistance over large distances will depend on the proportion of fields of a particular crop that are sprayed, and not only on within-field use strategies. The extent of any loss in fitness caused by the resistant mutation, and the effectiveness of the fungicide against the wild-type sensitive pathogen, also influence the speed that resistance will spread. It is suggested that some fields should be left untreated, or treated with different, non-cross-resistant fungicides. Both verification of the model and systematic commercialisation of such a 'patchwork' strategy will probably be difficult to achieve, although the authors point out that analogous non-Bt-treated refugia for Bt-sensitive insect populations have been established in Arizona through legislation.

Field experimentation on resistance management strategies is always a difficult task, requiring large, replicated plots, and sustained cropping, treatments and assessments for several successive years. Variation in infection conditions and disease pressure from year to year, irregular availability of adequate samples of the pathogen, movement of inoculum between plots, ingress of external inoculum into the

Cucumber powdery mildew caused by *Sphaerotheca fuliginea*. The healthy leaves were on a plant treated with dimethirimol via the roots. In this instance the mildew population was sensitive to dimethirimol, but resistant populations soon became common in some countries.
(Syngenta)

experimental area, and other difficulties often render such work inconclusive. An early field experiment on *Cercospora beticola* showed that alternation of benomyl and a tin fungicide delayed the development of benomyl resistance (Dovas *et al*., 1976). In several studies on cereal powdery mildews (*Blumeria graminis* f. sp. *tritici* and *hordei*), field application of mixtures of triazoles with morpholine or aminopyrimidine fungicides was found to hinder the development of resistance to one or to both of the fungicides applied, which did occur after sequential applications of each fungicide alone (Heaney *et al*., 1988; Brent *et al*., 1989; Lorenz *et al*., 1992). Effects of fungicide alternation were less regular, giving either a similar or a smaller benefit according to the particular study.

Development of resistance of *Botrytis cinerea* on tunnel-grown strawberries to dicarboximides, and of *Polyscytalum pustulans* and *Helminthosporium solani* on potatoes to thiabendazole, was shown to be delayed by the application of certain fungicide mixtures (Hunter *et al*., 1987; Carnegie *et al*., 1994). In experiments on grape powdery mildew (*Uncinula necator*) a mixture of triadimenol with sulphur or dinocap at roughly half normal rates did not slow down the evolution of triadimenol resistance; however, alternations, at full rates, did decrease resistance development (Steva, 1994). Build-up of QoI resistance in *Mycosphaerella graminicola* in field plots of wheat was much reduced by application of an azoxystrobin/epoxiconazole mixture, compared with a solo azoxystrobin treatment (Gisi *et al*., 2005). Overall, field experimentation does appear to support the adoption of mixture and rotation strategies, but since there are some inconsistencies and the range of diseases and fungicides worked on is rather limited, further work should be encouraged.

Practical experience also suggests that both mixture and rotation strategies have delayed resistance development, and examples are discussed later. However, fully conclusive evaluations of commercial-scale strategies are difficult to make because comparable 'non-strategy' areas have seldom existed.

2. Restrict the number of treatments applied per season, and apply only when strictly necessary. Use other fungicides both beforehand and subsequently

This approach, like rotation, reduces the total number of applications of the at-risk fungicide and therefore must slow down selection to some extent. It can also favour decline of resistant strains that have a fitness deficit. However, the treatments, which are still applied consecutively, generally coincide with the most active stages of epidemics when selection pressures are highest.

Thus any delay in resistance may not be proportional to the reduction in spray number. On the other hand a substantial break in use at a time when the pathogen is still multiplying can allow a beneficial resurgence of more sensitive forms. Examples are considered later.

3. Maintain manufacturers' recommended dose

For many years farmers have often used reduced rates of application of fungicides, mainly to reduce costs, especially in conditions where disease pressures are usually low, or where the risk of financial loss from reduced performance was not great. Also, advisory services in pursuing lower-input approaches for economic and environmental reasons, have recommended use of smaller doses for certain situations. On the other hand it is the view of FRAC that recommended doses must be maintained, not only because they will retain the built-in safety factor and secure the claimed levels of performance under a wide range of conditions, but more particularly because it is possible that reducing the dose could enhance the development of resistance.

However, relationships of fungicide dose to risks of resistance are not yet fully established, and it seems likely that they may vary according to the fungicide in question. Some of the models referred to above indicate that lowering the dose of the at-risk fungicide (but retaining normal spray frequency) can delay build-up of major-gene resistance by decreasing the overall effectiveness, increasing the numbers of sensitive survivors and hence slowing down the selection of resistant forms that can survive the full dose. With regard to multi-step resistance, it has been argued that lowering dose can enhance resistance development by favouring the survival of low-level resistant forms which would be inhibited by the full dose. The low-level resistant forms could then mutate further or recombine sexually to give higher levels of resistance. In practice the doses that actually reach the target organisms vary greatly over space and time, giving very complex mixes of different exposure sequences. Thus it can be argued equally that lowering the dose could hinder multi-step resistance by giving a fore-shortened range of concentrations that would not provide the step-ladder of selection pressure up to the highest levels. Moreover, as the dose rate approaches zero there certainly will be no selection for resistance.

Experimental data regarding effects of different doses are still rather limited and confusing. In a growth chamber experiment, selection for resistance to triazoles in barley powdery mildew was slowed down by lowering fungicide concentrations (Porras *et al*., 1990). Again the work is more difficult to do in the field, partly because

Apple leaves bearing lesions of scab disease, caused by Venturia inaequalis. Resistance to benzimidazoles and dodine has caused considerable problems in the control of this disease.
(K J Brent)

degrees of effectiveness, which must be critical, vary greatly between and within growing seasons. Decreasing application rates appeared to slow down development of resistance of triadimefon to barley powdery mildew (Hunter *et al*., 1984), but in other experiments on strawberry *Botrytis* and wheat eyespot altering fungicide doses made little difference to resistance build-up (Hunter *et al*., 1987; Hunter *et al*., 1993). When a benomyl-mancozeb mixture was applied to control apple scab, build-up of benomyl resistance was delayed by reducing the benomyl concentration and increasing the mancozeb concentration (Lalancette *et al*., 1987). Halving the rate of triadimenol enhanced development of resistance in grape powdery mildew in France (Steva, 1994), and 'split' (lower dose but more frequent) applications of fenpropimorph and fenpropimorph-propiconazole mixtures led to significant decreases in fenpropimorph sensitivity of wheat powdery mildew in Germany and Holland (Forster *et al*., 1994; Engels and De Waard, 1994). However, reducing the dose of fenpropimorph did not affect the sensitivity of barley powdery mildew in the UK (Zziwa and Burnett, 1994). Decreasing the dose of DMI fungicides from one-quarter to one-eighth of the full recommended dose was found to reduce resistance development in *Mycosphaerella graminicola* (Metcalfe *et al*., 2000; Mavroeidi and Shaw, 2006).

It is now widely accepted, on theoretical grounds, limited experimental data and practical experience, that risks of major-gene (single-step) resistance are unlikely to increase, and may well decline as dose is lowered. The situation with regard to polygenic resistance is still not at all clear, and more experimental work is justified in order to obtain a sounder base for recommendations. Some of the published data refer specifically to 'split' schedules, in which dose is lowered but frequency of application is correspondingly increased, to give the same total mount applied each season. It is important to distinguish these from reduced-dose applications made on normally timed schedules so that the total dose per season is decreased. The use of more frequent 'split' applications could increase resistance risk and should be avoided.

4. Avoid eradicant use

One of the advantages of systemic fungicides is that they can eradicate or cure existing infections. This property greatly assists their use on a 'threshold' basis, where application is made only when a certain, economically acceptable, amount of disease has already appeared, in order to prevent further spread. However, avoidance of the use of systemic fungicides in this way has been recommended in two different situations as an anti-resistance strategy.

FRAC has recommended that eradicant use of phenylamides should be avoided. This is because they are now always applied for control of foliage diseases as a mixture with a multi-site companion fungicide. The latter does not work as an eradicant, so that the phenylamide is acting alone when the mixture is applied to existing infections.

Avoidance of eradicant use could possibly delay resistance for another, more widely applicable reason. To wait until a threshold population of the pathogen appears, usually means that many sporulating lesions (occupying up to 5% of the foliar area) are exposed to the fungicide. Opportunity for selection could be much greater than if the fungicide had been applied prophylactically to keep populations permanently low. Presumably it is with this risk in mind that FRAC discourages the eradicant use of DMIs in some fruit crops. To the authors' knowledge there is no experimental evidence comparing the resistance risks of prophylactic versus threshold-based schedules, and research on this would be useful.

Storage rot of oranges caused by *Penicillium digitatum*. Resistance to phenols, benzimidazoles and sec-butylamine has caused problems, but the advent of newer fungicides and the adoption of resistance management programmes have enabled satisfactory control to be maintained overall. (J W Eckert, University of California)

5. Integrated disease management

This is a particular aspect of the concept more generally referred to as IPM (Integrated Pest Management). The integrated use of all types of countermeasures against crop disease is not only highly desirable on economic and environmental grounds, but is also a major strategy for avoiding or delaying fungicide resistance. The use of disease-resistant crop varieties, biological control agents, and appropriate hygienic practices, such as crop rotation and removal of diseased parts of perennial crop plants, reduces disease incidence and permits the more sparing use of fungicides, and in both these ways decreases selection of fungicide-resistant forms. Equally of course the application of fungicides reduces the risk of build-up of pathotypes with changed virulence and the consequent 'breakdown' of disease-resistant varieties.

Unfortunately, non-chemical methods of disease control are often weak or not available, so that fungicide application is the predominant or even the sole countermeasure for many diseases (e.g. potato late blight, grape downy mildew, Sigatoka disease of bananas, wheat bunt, stripe (yellow) rust of wheat, to name a few).

6. Chemical diversity

The availability of a number of different types of fungicide for the control of each major crop disease is highly beneficial both environmentally and in order to overcome resistance problems. The continued use of one or a very few types of compound over many years presents a much greater risk of side-effects and favours resistance in the

Late blight on potato foliage, caused by *Phytophthora infestans*. Although phenylamide – resistant forms are widespread, phenylamides are still used effectively in mixture or rotation with mancozeb and other fungicides.

target organisms. Thus it is crucial that chemical invention and new product development are sustained. Fortunately, registration authorities now accept the need for diversity, in terms of pesticide chemistry and mechanisms of action, provided that the new compounds maintain safety standards. A new fungicide does not necessarily have to be superior to existing ones in order to be of value. It has to be effective, and, in the resistance context, it should work against strains that are resistant to existing fungicides. This latter property is usually associated with a new mode of action, and ideally there should be more than one site of action to decrease the risk of evolution of resistance to the new fungicide.

However, the development of new, highly active members of an existing fungicide class, which retain the same primary mechanism of action, may also be of some use in resistance management. This is exemplified by the latest triazole fungicide prothioconazole, which is more potent generally and against which smaller resistance factors are exhibited (Kuck and Mehl, 2004). Its introduction has to some extent decreased problems of triazole resistance in cereal powdery mildews.

The withdrawal of fungicides, for example captafol and organo-tin fungicides, for safety reasons has been necessary from time to time, but it has reduced options for resistance avoidance strategies. It must be hoped that further de-registrations do not occur. Restrictions on the use of ethylenebisdithiocarbamates (EBDCs), such as mancozeb, already operate in several countries, and possibly these could become more widespread and severe. This is a worrying prospect with regard to fungicide resistance management. It is notable that in Sweden products based solely on EBDCs have been prohibited, whereas products containing EBDCs together with other fungicides can still be marketed and used.

IMPLEMENTATION OF MANAGEMENT STRATEGIES

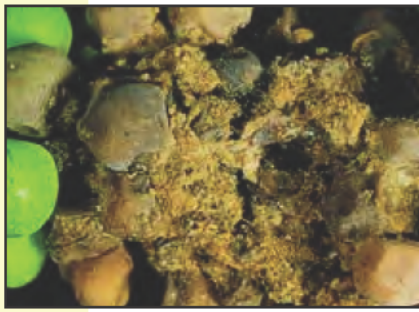
Whilst public-sector research and advisory organisations have contributed greatly to the establishment of countermeasures, the agrochemical industry has had to bear the major responsibility of planning and implementation, and of course the associated financial risks.

When fungicide resistance first emerged as a major problem, the manufacturers concerned had to respond as best they could against an unforeseen situation. Resistance to benzimidazoles arose in 1969-70, only one to two years after first introduction. The companies involved adopted a low-key approach, dealing with complaints on an ad-hoc basis, and placing general warnings of the existence of resistant strains and disclaimer notices on product labels. Results of any monitoring or other studies done by them at this time were not published for 10 years, and no recommendations regarding resistance management were issued.

Resistance to dimethirimol first appeared in Holland in 1970, the second year of use. With hindsight, the year-round, almost universal use of this highly specific, systemic fungicide, in glasshouses, to control the vigorous, abundantly sporulating cucumber powdery mildew, was the ideal scenario for resistance build-up. The manufacturing company mounted quickly a systematic monitoring programme (the first of its kind), obtained clear evidence of practical resistance, withdrew the product from use in affected regions, and published relevant data (Bent, *et al.*, 1971).

Signs of resistance of barley mildew to the related compound ethirimol subsequently were found in the UK, and the same manufacturer again published data as did the Plant Breeding Institute (PBI) at Cambridge (Shephard *et al.*, 1975; Wolfe and Dinoor, 1973). With advice from PBI, the company introduced a strategy of withdrawal of use from winter barley, to break the year-round cycle of use. The resistance did not worsen and a useful degree of disease control on spring barley was sustained. As more alternative treatments came into use in the late 1970s ethirimol application to winter barley was restored, and the level of resistance actually declined (Heaney *et al.*, 1986). Since the company concerned was the sole manufacturer of these two pyrimidine fungicides, it was possible to implement major changes in use strategies uniformly and without reference to other companies.

Carboxanilides and amines ('morpholines'), introduced at about the same time as the benzimidazoles and 2-amino-pyrimidines, did not encounter the rapid onset of major resistance problems. In 1980, however, strong resistance to metalaxyl, a relatively new Oomycete fungicide, occurred in certain countries, and signs of resistance to dicarboximides were also starting to appear. This situation of increasing concern prompted a group of industrial scientists, who were attending a fungicide resistance course at Wageningen in 1980, to propose the formation of an inter-Company Group that would cooperate in investigating resistance problems and establishing



Grapes infested by *Botrytis cinerea*. Resistance to benzimidazole and dicarboximides fungicides has affected control seriously in some regions. New fungicides appear promising.

countermeasures. At a meeting in Brussels in 1981, company representatives agreed a draft constitution and modus operandi for FRAC.

Since then FRAC has been very active in sharing confidential company information on the incidence of resistance, in planning relevant studies with agreed company inputs, and in issuing consensus recommendations for the agrochemical industry and for advisers and farmers (Russell, 2006).

FRAC decided to operate through Working Groups, one for each major class of fungicides to which resistance is known, and which has more than one manufacturer, or potential manufacturer with an announced development product. Currently there are four Working Groups, dealing with SBI (sterol biosynthesis inhibitor) fungicides, anilinopyrimidines, QoI (quinone outside inhibitor) fungicides and CAA (carboxylic acid amide) fungicides. These Groups collect and publish data on resistance status in different crops, pathogens and countries, and issue and review annually resistance management guidelines. Three former Working Groups, concerned with benzimidazoles, dicarboximides and phenylamides, have now converted to Expert Fora, giving relevant information and advice on request. The latest information and guidelines from each Working Group are available on the FRAC website (www.frac.info).

Benzimidazoles

Many pathogens adapted very quickly to benzimidazoles, for example *Botrytis* spp. Others took about 10 years before being detected e.g. *Oculimacula* spp., cause of cereal eyespot disease (Locke, 1986) or even 15 years (e.g. *Rhynchosporium secalis*, cause of barley leaf-scald (Kendall *et al*., 1993).

Over the years the use of mixtures or alternations with non-benzimidazole fungicides has been encouraged with varying degrees of vigour by the individual companies concerned and by advisory services. Often this was done too late. When benzimidazole resistance has already become established, it usually persists.

An example of the successful early use of a mixture strategy is the application of benzimidazoles to control *Cercospora* leaf-spots of peanut in the USA. In the southeastern states, where there was sole use of benomyl, practical resistance soon appeared. In Texas, where benzimidazole-mancozeb mixtures were used from the start, no resistance developed over many years except in trial plots where a benzimidazole

alone was applied repeatedly (Smith, 1988). The FRAC Working Group (now an Expert Forum) supported the use of mixtures or alternation in a general way, and the avoidance of eradicant use unless absolutely necessary, but did not make specific recommendations or initiate major monitoring projects.

Use of benzimidazole fungicides worldwide is still substantial, despite the widespread incidence of resistance since the early 1970s. In the absence of data it is hard to say to what extent benzimidazole fungicides are now still effective, and whether use on the present scale is fully justified. Monitoring in 1997-2003 in France revealed the common occurrence at high frequency of benzimidazole-resistant strains of *Mycosphaerella graminicola* and *Oculimacula* spp in wheat (Leroux *et al*., 2003, 2005 a). A comprehensive, up-to-date survey of the situation world-wide regarding the current use and effectiveness of benzimidazole fungicides would certainly be valuable.

One special and interesting approach to overcoming benzimidazole resistance has been the application of a mixture of the benzimidazole fungicide carbendazim with diethofencarb, to control *Botrytis* in grapes and other crops. Diethofencarb shows negative cross-resistance with respect to benzimidazoles. Remarkably, it inhibits only benzimidazole-resistant strains of the target pathogens and does not affect benzimidazole-sensitive strains. In practice a formulated carbendazim-diethofencarb mixture, introduced in 1987 initially gave good control of *Botrytis*, irrespective of whether pathogen populations were benzimidazole-resistant or not. However, the appearance and spread of strains resistant to both fungicides caused problems (Elad *et al*., 1992; Leroux and Moncomble, 1994) and the product is no longer used.

Phenylamides

These fungicides were first introduced in 1977. They act specifically against oomycete pathogens, having no effect on other classes of fungi.

In 1980 the first cases of resistance occurred, suddenly and seriously, against metalaxyl applied to cucumbers for control of downy mildew (*Pseudoperonospora cubensis*) in Israel and applied to potatoes in certain European countries for control of late blight (*Phytophthora infestans*). In the following year resistance appeared also in grape downy mildew (*Plasmopara viticola*) in France and South Africa and in tobacco blue mould (*Peronospora tabacina*) in Central America. These events were unexpected, since results of 'training' experiments done by the manufacturer (Staub *et*

Black Sigatoka disease of bananas caused by *Mycosphaerella fijiensis* var. *difformis*. Strains resistant to benzimidazoles, DMI and QoI fungicides have developed in some countries and have prompted the international adoption of agreed management strategies.
(K.J Brent)

al., 1979) had appeared to indicate a low degree of risk. The dramatic occurrence in 1980 of practical resistance problems, in such a promising new fungicide class which was beginning to involve other manufacturers, was perhaps the most compelling influence underlying the formation of FRAC.

Recognising that resistance in *Phytophthora infestans* was associated with the solo use of metalaxyl, and that it had not occurred in those countries where only formulated mixtures with mancozeb were applied, the manufacturer immediately withdrew the single product from use against foliar diseases and recommended that mixtures with multi-site fungicides should be used. Subsequently the FRAC Phenylamides Working Group produced a full set of guide-lines. In abbreviated form, these are:

- Use only as protectants; no curative or eradicant applications.
- For foliar application use only pre-packed mixtures with residual partner fungicide; the latter should be at ¾ to full dose, but the phenylamide dosage depends on the intrinsic activity and is defined by the respective company.
- Do not use soil treatments to control foliar disease.
- Limit sprays to 2-4 consecutive applications per crop per year; do not exceed 14 day intervals.
- Use in early season or period of active crop growth only, then switch to a non-phenylamide product.
- Do not use on seed potato crops or in nurseries.

Although not without difficult negotiation, FRAC secured uniform implementation of these guide-lines by all the companies involved, and major use of this class of fungicides continues against all target diseases. Since the problem of phenylamide resistance first arose, several effective new oomycete-active fungicides have been introduced, e.g. QoI fungicides, fluazinam, dimethomorph, cyazofamid and zoxamide, so that many more options for diversified application programmes now exist.

Application of the FRAC recommendations did not in fact delay for long the appearance and spread of resistant variants of *P. infestans*, which have become readily detectable in many crops in most countries of use. Nevertheless there is evidence from field experiments that phenylamide-mancozeb mixtures continue to perform better than mancozeb alone (Staub, 1994), even in re-entry situations where a phenylamide alone was originally used and then withdrawn (Dowley, 1994). The reasons for this are not fully understood. The use of a leaf-disc test with a multiple spore inoculum may

have over-estimated the frequency of resistant mutants within crops. Since the Oomycetes have multinucleate hyphal cells and sporangia, it is possible that the proportion of nuclei with a resistant gene is a critical factor (Cooke *et al*., 2006). The underlying reason for the sustained field activity of metalaxyl in mixtures, which has also been observed in the control of lettuce downy mildew, *Bremia lactucae* (Wicks *et al*., 1994), deserves more detailed study.

Against most Oomycete pathogens, chemical application is the only effective method of control and there is not much scope for the IPM approach. An exception is the downy mildew of lettuce. Metalaxyl-resistant populations of this fungus are composed only of one of a few particular pathotypes. Cultivars carrying genes for resistance specifically against one of these pathotypes have been deployed in combination with phenylamide treatment as a successful integrated control and resistance management strategy (Crute *et al*., 1994). Metalaxyl-resistant strains of a different pathotype do arise from time to time, so that sustained surveillance and modification of recommendations is necessary.

Dicarboximides

Fungicides of this class (iprodione, vinclozolin and procymidone) have been used since the mid-1970s mainly to control fungi of the related genera *Botrytis*, *Sclerotinia* and *Monilinia*. They largely replaced benzimidazole fungicides, which in many situations were no longer effective because of resistance. Dicarboximide-resistant variants appear frequently in laboratory cultures, and after about three years of intensive use, resistant strains were detected also in the field. The field isolates have shown differing degrees of resistance, and pathogenicity and other fitness factors tend to decline as the degree of resistance increased. The proportion of resistant strains varies greatly with time of year; they decline after dicarboximide treatment ceases and increase again when it is resumed. Practical control problems, associated with moderately resistant populations occurred, but at first were localised and variable in degree. During the 1980s difficulties gradually increased, especially in grape-vines in the parts of Europe where *Botrytis* is most prevalent, and even where mixtures were used control was sometimes inadequate.

The FRAC Dicarboximide Working Group made the following recommendations:

- Do not apply more than two or three times per crop per season.

- Save applications for times when *Botrytis* infection pressure is high.
- Leave prolonged periods without selection pressure.
- Where resistance is established use mixtures to stabilise *Botrytis* control, using the application rules given for a dicarboximide alone.

Despite extensive use of these guide-lines, practical resistance to different degrees became widespread in grape-vines, especially in parts of France, and a sporadic problem in some other crops. Earlier companion compounds such as captan, thiram, dichlofluanid and chlorothalonil did not give fully adequate control, alone or in mixture with a dicarboximide, but the restricted, once per year use of newer *Botrytis*-active fungicides such as fluazinam, fludioxonil, fenhexamid and the anilinopyrimidines, and also the dicarboximides, is now giving good levels of grape-vine *Botrytis* control in France (Leroux *et al*., 2005 b).

SBIs (sterol biosynthesis inhibitors)

This large class of fungicides comprises three distinct groups: the sterol C14-demethylation inhibitors (DMIs, e.g. triazoles, imidazoles, fenarimol, triforine); amines (morpholines e.g. tridemorph, fenpropimorph, piperidines e.g. fenpropidin, spiroketalamines e.g. spiroxamine); hydroxyanilides (e.g. fenhexamid).

DMIs were first used in the 1970s, triforine, triadimefon and imazalil being early representatives. Since then at least 30 more DMIs have been used in agriculture. At the time the FRAC Working Group formed, in 1982, there were very few reports of DMI resistance. They have a site-specific mode of action, and resistant mutants were easily obtained by mutagenic treatment in the laboratory. However, such mutants had reduced pathogenicity and other fitness attributes, so that development of practical resistance was deemed unlikely (Fuchs and Drandarevski, 1976). Practical resistance did in fact develop in several pathogens during the 1980s (e.g. powdery mildews, *Venturia inaequalis*, *Mycosphaerella fijiensis* var *difformis*), but relatively slowly and with fluctuating severity, as is considered to be characteristic of polygenic resistance.

Although amine fungicides have been used extensively for many years, they continue to perform well. Considering the amount of use, their potency, the high multiplication rates of the main target pathogens (e.g. powdery mildews and *Mycosphaerella. fijiensis* var *difformis*), and the ease of generating resistant mutants in the laboratory, the stability of their performance has been remarkable. Some reports of decreased

sensitivity have appeared from time to time. The slightly resistant field isolates were not cross-resistant to the DMI fungicides, which act at a different stage of sterol biosynthesis.

Interestingly, several studies have revealed cross-resistance between isolates of barley and wheat powdery mildews with respect to fenpropimorph and fenpropidin, but little cross-resistance to tridemorph appears to occur (Readshaw and Heaney, 1994). This pattern correlates well with information on mechanisms of action, since fenpropimorph and fenpropidin are considered mainly to inhibit the Δ14-15 reduction step, and tridemorph mainly the Δ8-7 isomerisation step, in sterol biosynthesis (Hollomon, 1994). However, there is evidence for additional sites of action, and a multi-site action, coupled with the flexible, multi-configurational nature of the carbon chain, could account for the durability of action of the morpholine fungicides.

Hydroxyanilide fungicides inhibit yet another step in sterol biosynthesis, catalysed by C3-keto-reductase. Fenhexamid, the sole hydroxyanilide in commercial use is applied specifically for control of *Botrytis* spp. and related pathogens. During eight years of use, no development of resistance to fenhexamid has been detected.

FRAC has made the following general recommendations regarding use of SBI fungicides:

- Do not use repeated applications of SBIs alone on the same crop in one season against a high-risk pathogen in areas of high disease pressure for that pathogen.
- For crop/pathogen situations requiring multiple spray applications, e.g. orchard crops/powdery mildews, use mixtures or alternate (in block sprays or in sequence) with effective non-cross-resistant fungicides.
- If mixture or alternation is not possible, reserve SBI use for the critical part of the season or critical crop growth stage.
- If DMI or amine performance declines and less sensitive forms of the pathogen are detected, SBIs should only be used in mixture or alternation with effective non-cross-resistant fungicides.
- Complementary use of other fungicide classes with different modes of action should be maximised.
- Use as recommended on the label. Do not use reduced doses.
- Use other measures such as resistant varieties, good agronomic practice, plant hygiene.

Recommendations for specific crop sectors have been made, and are published on the FRAC website. In general these confirm and amplify the above general recommendations. Eradicant use is discouraged in apples and grapes.

These recommendations have been widely implemented, and in general the SBI fungicides are continuing to give good control of most target pathogens some 30 years after their introduction. The warning against reduced rates could be open to debate since, as discussed earlier, the relevant experimental data are limited and conflicting. This is clearly an important area for further research. However, it is of course always necessary to use DMIs in amounts sufficient to ensure cost-effective disease control under the particular conditions of use.

Anilinopyrimidines

These fungicides, which include cyprodinil, pyrimethanil and mepanipyrim, act against a broad range of fungi. The FRAC Anilinopyrimidines Working Group has focussed mainly on resistance management in *Botrytis cinerea* and *Venturia inaequalis* on apple, which are high-resistance-risk pathogens and also important commercial disease targets for this fungicide class. Resistant strains of both pathogens have been detected in vineyards and apple orchards. These are cross-resistant to all the anilinopyrimidine fungicides, but not to other fungicide classes. They have remained at low frequency, and performance of anilinopyrimidines continues to be very good after twelve years of commercial use.

Guidelines for use have been published by FRAC and implemented throughout this period. These differ according to the crop disease, but the general approach is to restrict the number of anilinopyrimidine treatments to be applied per crop and season.

QoIs (Quinone outside Inhibitors, "strobilurins")

The class at present comprises twelve fungicides, from several different, but related chemical groups (e.g. methoxyacrylates, oximino acetates) which have a common mode of anti-fungal mode of action, inhibiting electron transfer at the Qo site in mitochondrial complex III. They were first introduced ten years ago, and have been widely used against a broad range of pathogens.

Within two years after their introduction, marked loss of action against powdery mildew, associated with development of highly resistant populations was observed in

wheat crops in Germany, and soon after throughout north-west Europe (Chin *et al*., 2001). Subsequently, serious resistant problems have been encountered in a range of target pathogens, for example *Mycosphaerella graminicola* (cause of leaf spot of wheat), *Plasmopara viticola* (downy mildew of grapes), *Venturia inaequalis* (cause of apple scab) and *Mycosphaerella fijiensis* var. *difformis* (cause of black Sigatoka disease of bananas). A full list, with literature citations is given by the QoI working group on the FRAC website. In general, resistant forms have shown cross-resistance to all the QoI fungicides. It is notable that resistance has not developed in *Phytophthora infestans* (cause of potato late blight), a major target for some QoIs. As with other fungicide classes, the occurrence of resistant strains, and associated losses of QoI performance, vary greatly between regions of use. For example, resistance of *Plasmopara viticola* is much more prevalent in northern and south-western France, than in Hungary or Spain where disease pressure and QoI use are generally lower.

According to recent FRAC reports, in seventeen pathogens a high level of resistance (resistance factor usually greater than 100) has been shown to be caused by a single mutation (G143A) in the cytochrome bc-1 gene. Another single mutation (F129L), generally causing a much lower degree of resistance, and little or no loss of control provided recommended application rates are adhered to, has been detected in three pathogens. Three further pathogens have produced strains with both these mutations. It is noticeable that QoI resistant oomycete pathogens are sensitive to cyazofamid, a QiI fungicide that blocks electron flow through the second quinone binding site of cytochrome bc-1 which faces the inside of the mitochondrial matrix (Mitani *et al*., 2005). Cyazofamid may be used as a partner to QoIs in resistance management programmes, although it should be recognised that both QoI and QiI fungicides activate alternative oxidase, which causes low levels of resistance to both fungicide groups (Wood and Hollomon, 2003; Hollomon *et al*., 2005; Gisi *et al*., 2005).

General FRAC guidelines for use of QoI fungicides include the following key instructions:

- Apply QoI fungicides at effective rates and intervals, according to manufacturers' recommendations.
- Limit the total number of applications within a total disease management programme, whether applied solo or in mixture with other fungicides.
- Alternate QoI applications, whether solo or in mixture, or whether single or block treatments, with applications of effective fungicides from other cross-

resistance groups. Specific recommendation on size of blocks are given for specific crops. Block applications of QoIs must only be made in mixture with a non-cross-resistant fungicide.

Specific recommendations for the use of QoIs in cereal crops, grapes and bananas are published on the FRAC website, In cereals and bananas, QoIs should always be used in mixtures with non-cross-resistant fungicides.

CAAs (carboxylic acid amides)

A FRAC Working Group has been established recently to promote and co-ordinate resistance management for the carboxylic acid amide (CAA) fungicides. At present those used commercially are dimethomorph, flumorph, benthiavalicarb, iprovalicarb and mandipropamid. They specifically act against oomycete pathogens, and probably have a common mode of action.

Shortly after the first CAA (dimethomorph) was introduced in 1993, and despite recommendations to always use in combination with multi-site fungicides, less sensitive populations of *Plasmopara viticola* were observed in a number of vineyards in France and Germany. Since then the frequency of less sensitive populations, and the degree of loss of sensitivity have fluctuated, with no clear progressive build-up of resistance in these or other regions. CAA resistance in *P. viticola* has been shown to be inherited in a recessive way (Gisi *et al*., 2007). This could limit its spread since oomycete fungi are diploid, or even polyploid, during much of their life cycle. Control appears to remain good, with no complaints received from growers, although it cannot be excluded that use of partner fungicides could in some situations mask a degree of loss of performance. No instances of reduced sensitivity have been shown in other oomycete pathogens, including *Phytophthora infestans* which has received extensive monitoring.

Thus CAAs are regarded by FRAC as moderate-risk fungicides, which should continue to perform well against all target diseases provided guidelines are followed. Key recommendations made by the Working Group for use against *Plasmopara viticola* are:

- Apply no more than four CAA sprays per season.
- Apply always in mixture with effective multi-site or other non-cross-resistant fungicides.

No specific recommendations have yet been made for use against *Phytophthora infestans* or other oomycete pathogens and users are encouraged to follow the manufacturers' recommendations.

Resistance management in banana production

The crucial role of frequent fungicide applications in banana plantations, the serious problems caused by benzimidazole resistance in the main pathogen, *Mycosphaerella fijiensis* var. *difformis*, and the importance of securing agreement regarding use strategies between major production companies in different countries, were all considerations that led to the formation of a special Working Group of FRAC concerned with fungicide use and resistance management in bananas. The Group includes a number of growers as well as agrochemical manufacturer members.

Table 3
Summary of FRAC recommendations for use of fungicides on Banana to control black sigatoka

Updated during the FRAC working group meeting (Orlando, Florida, USA, 1 2. Feb.2006)

Chemical class	Solo or mixtures	Alternation or blocks	Maximum number of applications	Spray timing
Demethylation inhibitors (DMI)	Both, mixtures preferred	Only in full alternation	8; not more than **50%** of total number of sprays	*
Amine fungicides	Both, mixtures preferred	Block of maximum 2 consecutive sprays, full alternation preferred	15; not more than **50%** of total number of sprays	No restrictions
Qo inhibitors (QoI)	Only in mixtures	Only in full alternation	3; not more than **33%** of total number of sprays	**
Anilinopyrimidines (AP)	Both, mixtures preferred	Only in full alternation	6; not more than **50%** of total number of sprays	No restrictions
Benzimidazoles (BCM)	Only in mixtures	Only in full alternation	3; not more than **33%** of total number of sprays	**

* Applications starting preferably at onset of annual disease progression curve
** Preferably at lower disease pressure; sprays must be separated by at least 3 months

Over the past twenty years the Group's guidelines have changed considerably, in response to the introduction of new fungicide classes and to the development of resistance to some classes of fungicides in certain countries, as shown by sensitivity monitoring and performance checks. Monitoring is mainly done by germination tests, performed locally, and for QoIs additionally by PCR tests for the G143A mutation. Resistance problems have arisen with benzimidazoles, in all regions, and to some extent with DMI and QoI fungicides, mostly in Costa Rica and Panama. No problems have arisen so far with amines and anilinopyrimidines.

Specific guidelines vary according to the fungicide class, and key recommendations are given in Table 3. General guidelines, applicable to all groups, emphasise well-established points of good resistance management discussed above, but one distinct recommendation is that site-specific fungicides must be applied in oil or oil-water emulsions. These enhance fungicidal action and also exert an independent effect on black Sigatoka disease.

THE FUTURE

Whilst by no means fully successful, fungicide resistance management has undoubtedly prevented or delayed potentially more serious losses of disease control than those which have actually occurred. When practical resistance develops, it is now recognised and acted upon promptly, so that the wasteful use of ineffective treatments is avoided. Both FRAC and public-sector workers have had major roles to play in developing and implementing resistance management and will continue to do so.

Important new fungicide groups continue to emerge from the industrial laboratories, and of course it is vital to conserve their badly needed activities. It is also important that resources are made available to support the search for new modes of action, which will remain a cornerstone in resistance management. As fundamental research in genetics, biochemistry and epidemiology increase understanding of factors that influence risk, it should be possible to target the search for new modes of action involving inhibition of metabolic processes that offer low risk of resistance developing.

It is heartening to know that baseline studies, and other appraisal and strategy-making activities, are now firmly embedded in the evaluation and development of new fungicides within the individual companies concerned. It is vital that FRAC Working Groups for new fungicide classes should be formed at an early stage for all classes where more than one company is involved. The formation of the anilinopyrimidine and CAA Working Groups, before any practical resistance problems have arisen in these classes of fungicides, are encouraging examples.

In Europe many registration authorities now require protocols for sensitivity test methods, base-line data on the original range of sensitivity, and a statement on resistance risk assessment and management strategy, as part of the registration 'package' (Heimbach *et al*., 2002). Since such information should now be available, and since evidence for efficacy is already a registration requirement, these requirements seem quite reasonable. EU Directive 91-414 sets out the appropriate data requirements and FRAC (and other RACs) have worked closely with EPPO to produce a set of Guidelines (EPPO, 2002) to help in the gathering and interpretation of the necessary data. Also, submission of protocols regarding resistance management is a useful discipline for a company to undergo, and leads to an increased understanding amongst authorities of the problems of resistance management and their avoidance.

There remains a danger, however, of inflexibility through over-emphasis on rigid registration requirements. As experience of use of a new product grows, it may be necessary to change the accepted strategy quickly, and it is essential that this is not inhibited by bureaucratic delays. Any official categorisation of fungicide application to crops, as low-risk, high-risk etc., should be avoided, in view of the present uncertainty of knowledge regarding prediction of resistance development and effectiveness of management strategies, and the known variations in resistance development according to conditions of use in different regions. Of great help, as discussed earlier, would be a more rapid and positive response of registration authorities to new types of fungicides, which will increase diversity. A more positive response of some authorities to applications for registration of pre-packed mixtures will also help resistance management.

From time to time individual companies sponsor research projects concerning fungicide resistance. However, there is scope for a stronger and more sustained interaction between FRAC and public-sector researchers and advisers, and for industrial funding of research projects. A difficulty regarding research projects is that

Germ-tube growth test on sensitive strain of *Mycosphaerella fijiensis* var. *difformis* (banana black Sigatoka disease pathogen). Spores in the top photograph exposed to 5 ppm benomyl. (FRAC)

one company may not wish to fund jointly research in which the model compound belongs to another company. Also a company may not wish its compound to be the subject of an investigation in case undesirable results are obtained. These difficulties may prove hard to overcome in some situations.

There are also opportunities for funding of resistance research by growers through levy-funded organisations, which is very appropriate and should be encouraged world-wide. But national grower organisations can be wary of supporting fungicide research that may also aid production in other countries. It may be possible to obtain funds for resistance management projects in developing countries through the international aid agencies, provided that deserving proposals can be formulated.

Further research is still badly needed on the field behaviour or 'epidemiology' of resistant biotypes, on the biochemical and genetic basis of resistance, and on their interaction with different use strategies. This will provide a sounder basis for effective resistance management, which still depends too much on opinion. Effects of altering dose, both on normal and 'split' schedules particularly require more study, with respect to discrete and multi-step resistance. Genetic evidence for the important concepts of major-gene and polygenic resistance is based largely on studies of laboratory mutants, and more work on field isolates remains a priority.

In the past much monitoring work, particularly that done by industry, has not been fully published. Such information, including base-line data, is of long-term value and is now more often published in scientific journals, or summarised on the FRAC web site (www.frac.info/publ) where status reports and recommendations are also published regularly. A Resistant Pest Management Newsletter is published by Michigan State University (www.whalonlab.msu.com/rpmnews), but the emphasis is strongly on insecticide resistance. Communication and discussion of results and recommendations through occasional symposia, workshops and training courses on fungicide resistance and its management must continue. The role of FRAC in this has been important and one hopes that it will be sustained. Use of the internet to transmit information rapidly to users world-wide, has quickly become a key component keeping growers and users up-to-date with resistance management approaches.

The provision of crop varieties with improved disease resistance, and the development of biological control agents will surely advance, and will strengthen the IPM approach. Care will be needed to maintain the effectiveness of these biological components of IPM, with use of similar strategies to those used for chemicals. The ability of

pathogens to overcome varietal resistance is well recognised, and the development of resistance of a fungal pathogen (*Botrytis cinerea*) to a biological control agent (*Bacillus subtilis* CL27) has been observed (Li and Leifert, 1994).

Where resistance can be shown to result from specific DNA changes in resistant isolates, various PCR diagnostic methods become the choice way to monitor resistance. Management of QoI anti-resistance strategies relies almost entirely on PCR diagnostics, and similar methods could be used to monitor resistance to benzimidazoles, dicarboximides, DMIs, and MBI-D fungicides. It is not only important that researchers keep abreast of advances in real-time PCR and array technologies, but sufficient resources must be made available for laboratories involved in routine monitoring to keep their instrumentation up-to-date in order to obtain the benefits of these developments, such as the greatly increased sample throughput, and rapid delivery of results. However, bioassay protocols, which can also be improved (Fraaije *et al*., 2005), must remain a component of monitoring programmes, since resistance may emerge through selection of different target site mutations, or completely different mechanisms.

There is no doubt at all that chemical control methods will always be required to maintain reliable crop yields of good quality. To conserve the fine fungicides we already have, and to protect new arrivals, attention to resistance management, and work to further improve it, must continue. Increased research effort, increased interaction between industry, public-sector research and advisory services, and registration authorities, and increased publication of information, will all be beneficial. However, moderation should be the keynote, since the lion's share of tight R & D budgets must go to new invention in chemical and biological crop protection.

ACKNOWLEDGEMENT

We are grateful to all those people who have assisted in various ways in the preparation of this second edition of this monograph. We must thank especially Professor Phil Russell, Professor Ulrich Gisi and Dr Karl Heinz Kuck for their most helpful support and advice.

REFERENCES

Anon. (1979) Pest resistance to pesticides and crop loss assessments, FAO Plant Protection and Production Paper 6/2 AGP: 1979/M/2, Rome, 41.

Anon. (1991) FRAC methods for monitoring fungicide resistance. EPPO Bulletin 21: 291 354.

Anon. (1992) FRAC methods for monitoring the sensitivity of fungal pathogens to phenylamide fungicides. EPPO Bulletin 22: 297 322.

Bent, K J, Cole, A M, Turner, J A W and Woolner, M (1971) Resistance of cucumber powdery mildew to dimethirimol. Proceedings 6th British Insecticide and Fungicide Conference, 274 282.

Birch, C P D and Shaw, M W (1997) When can reduced doses and pesticide mixtures delay the build up of pesticide resistance? A mathematical model. Journal of Applied Ecology 34: 1032 1042.

Brent, K J (1982) Case study 4: Powdery mildews of barley and cucumber. In: Fungicide Resistance in Crop Protection, Dekker, J and Georgopoulos, S G eds. Pudoc, Wageningen, 219 230.

Brent, K J (1986) Detection and monitoring of resistant forms: an overview. In: Pesticide Resistance: Strategies and Tactics for Management. National Academy Press, Washington DC, 298 312.

Brent, K J (1987) Fungicide resistance in crops: its practical significance and management. In: Rational Pesticide Use. Brent, K J and Atkin, R K eds. Cambridge University Press, 137 152.

Brent, K J (1995) Fungicide resistance in crop pathogens: How can it be managed? FRAC Monograph No 1, GIFAP, Brussels, 48pp.

Brent, K J, Carter, G A, Hollomon, D W, Hunter, T, Locke, T and Proven, M (1989) Factors affecting build up of fungicide resistance in powdery mildew in spring barley. Netherlands Journal of Plant Pathology 95: 31 41.

Brent, K J and Hollomon, D.W (1998) Fungicide resistance: The assessment of risk FRAC Monograph No 2, Global Crop Protection Federation, Brussels, 48pp.

Brent, K J, Hollomon, D W and Shaw M W (1990) Predicting the evolution of fungicide resistance. In: Managing Resistance to Agrochemicals, Green, M B, LeBaron, H M and Moberg, W K eds. American Chemical Society Washington DC, 303 319.

Brent, K J and Hollomon, D.W (2007) Fungicide resistance: The assessment of risk FRAC Monograph No 2, second revised edition, FRAC, 52pp.

Brown, J K M, Jessop A C, Thomas, S and Rezanoor, H N (1992) Genetic control of the response of *Erysiphe graminis* f.sp. *hordei* to ethirimol and triadimenol. Plant Pathology 41: 126 135.

Carnegie, S F, Cameron, A M, Hide, G A and Hall, S M (1994) The occurrence of thiabendazole resistant isolates of *Polyscytalum pustulans* and *Helminthosporium solani* on seed potato tubers in relation to fungicide treatment and storage. Plant Pathology 43: 961 971.

Chin, K M, Chavaillaz, D, Käsbohrer, M, Staub, T and Felsenstein, F g (2001) characterizing resistance risk of *Erysiphe graminis* f. sp. *tritici* to strobilurins. Crop Protection 20: 87 96.

Collina, M, Landi, L, Guerrini, P, Branzanti, M B and Brunelli, A (2005) QoI resistance of *Plasmopara viticola* in Italy: biological and quantitative real time PCR approaches. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton UK, 81 88.

Cooke, L R, Carlisle, D J, Donaghy, C, Quinn, M, Perez, F M and Deahl, K L (2006) The Northern Ireland *Phytophthora infestans* population 1998 2002 characterised by genotypic and phenotypic markers. Plant Pathology 55: 320 330.

Crute, I R, Gordon P L and Moss, N A (1994) Variation for response to phenylamides in UK populations of *Bremia lactucae* (lettuce downy mildew) and *Peronospora parasitica* (brassica downy mildew). In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 155 162.

Davidse, L C (1981) Resistance to acylalanine fungicides in *Phytophthora megasperma* f.sp. medicaginis. Netherlands Journal of Plant Pathology 87: 11 24.

Dekker, J (1982) Countermeasures for avoiding fungicide resistance. In: Fungicide 46 Resistance in Crop Protection, Dekker, J and Georgopoulos, S G eds. Pudoc, Wageningen, Netherlands, 177 186.

Delp, C J and Dekker, J (1985) Fungicide resistance: definitions and use of terms. EPPO Bulletin 15: 333 335.

De Waard, M A (1994) Resistance to fungicides which inhibit sterol 14a demethylation, an historical perspective. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E, and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 3 10.

De Waard, M A, Andrade, A C, Hayashi, K, Schoonbeek, H J, Stergiopoulos, I and Zwiers L H (2006) Impact of fungal drug transporters on fungicide sensitivity, multidrug resistance and virulence. Pest Management Science 62: 195 207.

Dovas, C, Skylakakis, G and Georgopoulos S G (1976) The adaptability of the benomyl resistant population of *Cercospora beticola* in Northern Greece. Phytopathology 66: 1452 1456.

Dowley, L J (1994) Practical aspects of phenylamide resistance management. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E, Parry, D W, eds. British Crop Protection Council, Farnham, Surrey, 147 154.

Eckert, J W (1982) Case study 5: Penicillium decay of citrus fruits. In: Fungicide Resistance in Crop Protection, Dekker, J and Georgopoulos, S G eds. Pudoc, Wageningen, 231 250.

Elad, Y, Yunis, H and Katan, T (1992) Multiple fungicide resistance to benzimidazoles, dicarboximides and diethofencarb in field isolates of *Botrytis cinerea* in Israel. Plant Pathology 41: 41 46.

Engels, A J G and De Waard, M A (1994) Effect of different treatment schedules on the sensitivity of *Erysiphe graminis* f.sp. tritici. to fenpropimorph. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Surrey, 303 308.

EPPO (2002) EPPO Standard PP 1/213(2) Efficacy evaluation of plant protection products: resistance risk analysis.

Forster, B, Chavaillaz, D, Steden, C, Radtke, W, Kasbohrer, M and Kuhl, A (1994) Influence of split application of fenpropimorph mixtures on disease control In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 331 335.

Fraaije, B A, Butters, J A, Coelho, J M, Jones, D R and Hollomon, D W (2002) following the dynamics of strobilurin resistance in *Blumeria graminis* f.sp. *tritici* using quantitative allele specific real time PCR measurements with the fluorescent dye SYBR green. Plant Pathology 51: 45 54.

Fraaije, B A, Burnett, F J, Clark, W S, Motteram, J and Lucas, J A (2005) Resistance development to QoI inhibitors in populations of *Mycosphaerella graminicola* in the UK. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton UK, 63 71.

Fry, W E and Milgroom, M G (1990) Population biology and management of fungicide resistance. In: Managing Resistance to Agrochemicals, Green, M B, LeBaron, H M and Moberg, W K eds. American Chemical Society, Washington DC, 275 285.

Fuchs, A and Drandarevski, C A (1976) The likelihood of development of resistance to systemic fungicides which inhibit ergosterol biosynthesis. Netherlands Journal of Plant Pathology 82: 85 87.

Genet, J L, Jaworska, G and Deparis, F (2006) Effect of dose rate and mixtures of fungicides on selection for QoI resistance in populations of *Plasmopara viticola*. Pest Management Science 62: 188 194.

Georgopoulos, S G (1994) Early evaluation of fungicide resistance risk. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 389 396.

Giannopolitis, C N (1978) Occurrence of strains of *Cercospora beticola* resistant to triphenyltin fungicides in Greece. Plant Disease Reporter 62: 205 208.

Gilpatrick, J D (1982) Case study 2: Venturia of pome fruits and Monilinia of stone fruits. In: Fungicide Resistance in Crop Protection, Dekker, J and Georgopoulos, S G eds. Pudoc, Wageningen, 195 206.

Gisi, U and Staehle Csech, U (1988a) Resistance risk evaluation of new candidates for disease control. In: Fungicide Resistance in North America, Delp, C J ed. American Phytopathological Society, St Paul, Minnesota, 101 106.

Gisi, U and Staehle Csech, U (1988b) Resistance risk evaluation of phenylamide and EBI fungicides. Proceedings 1988 Brighton Crop Protection Conference Pests & Diseases, 359 366.

Gisi, U, Sierotzki, H, Cook, A and McCaffery, A (2002) Mechanisms influencing the evolution of resistance to QoI inhibitor fungicides. Pest Management Science 58: 859 867.

Gisi, H, Pavic, L, Stanger, C, Hugelshofer, H and Sierotzki, H (2005) Dynamics of *Mycosphaerella graminicola* populations in response to selection by different fungicides. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton UK., 89 101.

Gisi, U, Waldner, M, Kraus, N, Dubuis, P H and Sierotzki, H (2007). Inheritance of resistance to carboxylic acid amide (CAA) fungicides in *Plasmopara viticola*. Plant Pathology 56: 199 208.

Grasso, V, Palermo, S, Sierotzki H, Garibaldi, A and Gisi,U (2006). Cytochrome *b* gene structure and consequences for resistance to Qo inhibitor fungicides in plant pathogens. Pest Management Science 62: 465 472.

Heaney, S P, Hutt, R T and Miles, V G (1986) Sensitivity to fungicides of barley powdery mildew populations in England and Scotland; status and implications for fungicide use. Proceedings 1986 British Crop Protection Conference Pests & Diseases, 793 800.

Heaney, S P, Martin, T J and Smith, J M (1988) Practical approaches to managing anti resistance strategies with DMI fungicides. Proceedings 1988 Brighton Crop Protection Conference Pests & Diseases, 1097 1106.

Heaney, S P, Hall, A A, Davis, S A and Olaya, G (2000) Resistance to fungicides in the QoI STAR cross resistance group: current perspectives. Proceedings British Crop Protection Conference Pests & Diseases 755 762.

Heimbach, U, Kral, G and Niemann, P (2002) EU regulatory aspects of resistance risk assessment. Pest Management Science 58: 935 938.

Hilber, U W, Schuepp, H and Schwinn, F J (1994) Resistance risk evaluation of fludioxonil, a new phenylpyrrole fungicide. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon D W, Smith, M, Russell, P E and Parry D W eds. British Crop Protection Council, Farnham, Surrey, 397 402.

Hollomon, D W (1981) Genetic control of ethirimol resistance in a natural population of *Erysiphe graminis* f.sp. *hordei*. Phytopathology 71: 536 540.

Hollomon, D W (1994) Do morpholine fungicides select for resistance? In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon D W, Smith, M, Russell, P E and Parry D W eds. British Crop Protection Council, Farnham, Surrey, 281 289.

Hollomon, D W, Butters, J and Clark, J (1984) Genetic control of triadimenol resistance in barley powdery mildew. Proceedings 1984 British Crop Protection Conference, Pests & Diseases, 477 482.

Hollomon, D W, Wood, P M, Reeve, C and Miguez, M (2005) Alternative oxidase and its impact on the activity of Qo and Qi site inhibitors. In Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton UK, 55 62.

Hunter, T, Brent, K J and Carter G A (1984) Effects of fungicide regimes on sensitivity and control of barley mildews. Proceedings 1984 British Crop Protection Conference Pests & Diseases, 471 476.

Hunter, T, Brent, K J, Carter, G A and Hutcheon, J A (1987) Effects of fungicide spray regimes on incidence of dicarboximide resistance in grey mould (*Botrytis cinerea*) on strawberry plants. Annals of Applied Biology 110: 515 525.

Hunter, T, Arnold, G, Jordan, V W L and Brent, K J (1993) Effects of different fungicide programmes on infection of wheat crops by *Pseudocercosporella herpotrichoides* and on build up of fungicide resistance, In: Proceedings 10th International Symposium on Systemic Fungicides and Antifungal Compounds, Lyr, H and Polter, C eds. Ulmer, Stuttgart, 165 174.

Kaku, K, Takagaki, M, Shimizu, T and Nagayama, K (2003) Diagnosis of dehydratase inhibitors in melanin biosynthesis inhibitor (MBI D) resistance by primer introduced restriction enzyme analysis in scylatone dehydratase gene of *Magnaporthe grisea*. Pest Management Science 59: 843 846.

Kato, T (1988) Resistance experiences in Japan. In: Fungicide Resistance in North America, Delp, C J ed. American Phytopathological Society, St Paul, Minnesota, 16 18.

Kendall, S, Hollomon, D W, Ishii, H and Heaney, S P (1993) Characterisation of benzimidazole resistant strains of *Rhynchosporium secalis*. Pesticide Science 40: 175 181.

Kianianmomeni, A, Felsenstein, F, Schwarz, G and Wenzel, G (2006) Validation of a real time PCR assay for the quantitative detection of strobilurin resistance in field isolates of *Pyrenophora teres*. (2007) Pest Management Science 63: 219 224.

Kuck, K H and Mehl, H (2004) Prothioconazole: sensitivity profile and anti resistance strategy. Pflanzenschutz Nachrichten Bayer 57: 225 236.

Kuck, K H (2005) Fungicide resistance management in a new regulatory environment. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton UK., 35 43.

Lalancette, N, Hickey, K D and Cole, H (1987) Effects of mixtures of benomyl and mancozeb on build up of benomyl resistant *Venturia inaequalis*. Phytopathology 77: 86 91.

Leroux, P and Moncomble, D (1994) Resistance of *Botrytis cinerea* to dicarboximides, benzimidazoles and phenylcarbamates in the Champagne vineyards. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 267 270.

Leroux, P, Fritz, R, Debieu, Albertini, C, Lanen, C Bach, J, Gredt, M and Chapeland, F (2002) Mechanism of resistance to fungicides in field strains of *Botrytis cinerea*. Pest Management Science 58: 876 888.

Leroux, P, Albertini, C, Arnold, A and Gredt, M (2003) Le piétin verse: caractéristiques et distribution des souches de *Tapesia acuformis* et *Tapesia yalundae* resistantes aux fungicides. Phytoma 557: 8 13.

Leroux, P, Gredt, M, Walker, A S, Monard , J M and Caron, D (2005a) Resistance of the wheat leaf blotch pathogen *Septoria tritici* to fungicides in France. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton, UK, 115 124.

Leroux, P, Gredt, M, Walker, A S and Panon, M L (2005b) Evolution of resistance of *Botrytis cinerea* to fungicides in French vineyards.

Li, H and Leifert, C (1994) Development of resistance in Botryotinia fuckeliana (de Bary) Whetzel against the biological control agent *Bacillus subtilis* CL27. Zeitschrift fur Pflanzenkrankheiten und Pflanzenschutz 101: 414 418.

Locke, T (1986) Current incidence in the UK of fungicide resistance in pathogens of cereals. Proceedings 1986 British Crop Protection Conference, Pests & Diseases, 781 786.

Lorenz, G (1988) Dicarboximide fungicides: history of resistance development and monitoring methods. In: Fungicide Resistance in North America, Delp, C J ed. American Phytopathological Society, St Paul, Minnesota, 45 51.

Lorenz, G, Saur, R, Schelberger, K, Forster, B, Kung, R, and Zobrist, P (1992). Long term monitoring results of wheat powdery mildew sensitivity towards fenpropimorph and strategies to avoid the development of resistance. Proceedings 1992 Brighton Crop Protection Conference Pests & Diseases, 171 176.

Mavroedi, V I and Shaw, M W (2006) Effects of fungicide dose and mixtures on selection for triazole resistance in *Mycosphaerella graminicola* under field conditions. Plant Pathology 55: 715 725.

McCartney, H A, Foster, S J, Fraaije, B A and Ward E (2003) Molecular diagnostics for fungal plant pathogens. Pest Management Science 59: 129 142.

Metcalfe, R J, Shaw, M W and Russell, P E. (2000) The effect of dose and mobility on the strength of selection for DMI fungicide resistance in inoculated field experiments. Plant Pathology 49: 546 557.

Mitani, S, Araki, S, Takii, Y, Oshima, T, Matsuo, N and Takeda, R (2001) The biochemical mode of action of the novel selective fungicide cyazofamid: specific inhibition of mitochondrial Complex III in *Pythium spinosum*. Pesticide Biochemistry and Physiology 71: 107 115.

Noble, M, Maggarvie, Q D, Hams, A F and Leaf, L L (1966) Resistance to mercury of *Pyrenophora avenae* in Scottish seed oats. Plant Pathology 15: 23 28.

Parnell, S, van der Bosch, F and Gilligan, C A (2006) Large scale fungicide spray heterogeneity and the regional spread of resistant pathogen strains. Phytopathology 96: 549 555.

Porras, L, Gisi, U, and Staehle Csech, U (1990) Selection dynamics in triazole treated populations of *Erysiphe graminis*. Proceedings 1990 Brighton Crop Protection Conference, Pests & Diseases, 1163 1168.

Readshaw, A E and Heaney, S P (1994) Fenpropimorph sensitivity in *Erysiphe graminis* f.sp. *tritici*; survey of northern France 1991 1993. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 297 302.

Russell, P.E (2003) Sensitivity baselines in fungicide resistance research and management. FRAC Monograph No 3. CropLife International, Brussels, 56 pp.

Russell, P E. (2006) Fungicide Resistance Action Committee (FRAC) Outlooks on Pest Management. 17:(3) 119 121.

Samoucha, Y and Gisi, U (1987) Use of two or three way mixtures to prevent build up of resistance to phenylamide fungicides in *Phytophthora* and *Plasmopara*. Phytopathology 77: 1405 1409.

Sanglard, D, Ischer, F, Koymans, L and Billie, J (1998) Amino acid substitutions in the cytochrome P450 lanosterol 14α□demethylase (*CYP51A1*) from azole resistant *Candida albicans* clinical isolates contribute to resistance to anti fungal agents. Antimicrobial Agents and Chemotherapy 42: 241 253.

Sierotzki, H, Kraus, N, Assemat, P, Stanger, C, Cleere, S, Windass, J and Gisi, U (2005) Evolution of resistance to QoI fungicides in *Plasmopara viticola* populations in Europe. In: Modern fungicides and anti fungal compounds IV. Dehne, H W, Gisi, U, Kuck, K H, Russell, P E and Lyr H eds. BCPC, Alton, UK, 73 88.

Schwinn, F J and Morton, H V (1990) Antiresistance strategies: design and implementation in practice. In: Managing Resistance to Agrochemicals, Green, M B. LeBaron, H M, and Moberg, W K eds. American Chemical Society, Washington DC, 170 183.

Shephard, M C, Bent, K J, Woolner, M and Cole, A M (1975) Sensitivity to ethirimol of powdery mildew from UK barley crops. Proceedings 8th British Crop Protection Conference, 59 60.

Smith, C M (1988) History of benzimidazole use and resistance. In: Fungicide Resistance in North America, Delp, C J ed. American Phytopathological Society, St Paul, Minnesota, 23 24.

Staub, T (1991) Fungicide resistance: practical experience with antiresistance strategies and the role of integrated use. Annual Reviews of Phytopathology 29: 421 442.

Staub, T (1994) Early experiences with phenylamide resistance and lessons for continued successful use. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E, Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 131 138.

Staub, T, Dahmen, H, Urech, P A and Schwinn, F (1979) Failure to select for *in vivo* resistance in *Phytophthora infestans* to acylalanine fungicides. Plant Disease Reporter 64: 385 389.

Staub, T and Sozzi, D (1984) Fungicide resistance: a continuing challenge. Plant Disease 68:1026 1031.

Steva, H (1994) Evaluating anti resistance strategies for control of *Uncinula necator*. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 59 66.

Wicks, T G, Hall, B and Pezzaniti, P (1994) Fungicidal control of metalaxyl insensitive strains of *Bremia lactucae* on lettuce. Crop Protection 13: 617 624.

Windass, J D, Heaney, S P, Renwick, A, Whitcombe, D M, Little, S, Gibson, N J, Theaker, J and Stanger, C P (2000) Methods for detecting low frequencies of mutations in mitochondrially encoded genes. International patent WO 00/66773.

Wolfe, M S and Dinoor, A (1973) Pathogen response to fungicide use. Proceedings 7th British Insecticide and Fungicide Conference, 813 822.

Wood, P M and Hollomon, D W (2003) A critical evaluation of the role of alternative oxidase in the performance of strobilurin and related fungicides acting at the Qo site of complex III. Pest Management Science 59: 499 511.

Yamaguchi, J and Fujimura, M (2005) Recent topics on action mechanisms of fungicides. Journal of Pesticide Science 30 : 67 74.

Zziwa, M C N and Burnett, F J (1994) The effect of reduced doses on the sensitivity of powdery mildew to fenpropimorph in barley field trials. In: Fungicide Resistance, Heaney, S, Slawson, D, Hollomon, D W, Smith, M, Russell, P E and Parry, D W eds. British Crop Protection Council, Farnham, Surrey, 303 308.

Keith J Brent OBE PhD FIBiol FRAgS

After graduating at London University in Botany and Microbiology, Keith Brent worked for over twenty years in ICI, now Syngenta. At first he studied the biochemistry of filamentous fungi, at the Akers Research Laboratories, Welwyn.

In 1964 he moved to Jealott's Hill Research Station where he led research on fungicides discovery and development and tackled some of the initial problems of fungicide resistance. In 1979 he was appointed Head of the Crop Protection Division at Long Ashton Research Station, University of Bristol, where he also became Deputy Director.

During this period he continued to be involved in fungicide research, and also taught in international courses on fungicide resistance in seven countries world wide.

Since 1992 he has worked as an international consultant in crop protection and agricultural research management and in 1995 he authored the first FRAC Monograph.

Derek W Hollomon PhD

Having gained a degree in Agricultural Botany at Reading University, Derek Hollomon started his plant pathology research at Hull University and was awarded a doctorate in 1965. After several years of post doctoral research in Canada, Australia and the USA, he returned to the UK to initiate research at Rothamsted on the mode of action of the systemic fungicides that were then beginning to be used for cereal disease control. His research soon extended to resistance problems, and these have continued to be a major interest since he moved to the Long Ashton Research Station in 1985.

His work has involved much collaboration with the agrochemical industry, and also has kept him in close contact with the growers. He was awarded the British Crop Protection Council Medal in 1995.

Since 2002, he has been a visiting fellow in the Biochemistry department of the University of Bristol researching the pathway of respiration in pathogenic fungi. He is technical editor of the journal Pest Management Science.

Reference 5

Footnote: 19

FRAC
FUNGICIDE RESISTANCE ACTION COMMITTEE

Purpose

FRAC is a Specialist Technical Group of CropLife International
(Formerly Global Crop Protection Federation, GCPF).

The purpose of FRAC is to provide fungicide resistance management guidelines to prolong the effectiveness of "at risk" fungicides and to limit crop losses should resistance occur.

The main aims of FRAC are to:

1. Identify existing and potential resistance problems.
2. Collate information and distribute it to those involved with fungicide research, distribution, registration and use.
3. Provide guidelines and advice on the use of fungicides to reduce the risk of resistance developing, and to manage it should it occur.
4. Recommend procedures for use in fungicide resistance studies.
5. Stimulate open liason and collaboration with universities, government agencies, advisors, extension workers, distributors and farmers.

Organisation Structure

FRAC is comprised of a Central Steering Committee, five Working Groups and three Expert Fora. The chairperson of each working group and expert forum are automatic members of Steering Committee.

Why FRAC ?

Fungicides have become an integral part of efficient food production. The loss of a fungicide to agriculture through resistance is a problem that affects us all. It may lead to unexpected and costly crop losses to farmers causing local shortages and increased food prices. Manufacturers lose revenue vital for funding the enormous development costs of new products. Without reinvestment there would be no new compounds. This would cause serious disease management problems that would endanger the world food supply.

The problem of resistance has increased since the advent of highly effective compounds with specific sites of action. Although representing marked improvements in performance, including systemic and therapeutic properties, experience has shown that these compounds may be prone to resistance. As reliance on these fungicides grows, action is required to safeguard their effectiveness.

Industry recognises its responsibilityin safeguarding new chemistries that are brought to market. Through FRAC and the Working Groups it coordinates, companies are striving to establish more effective communications to alert all people involved in the research, production, marketing, registration and use of fungicides to the problems of resistance.

With an enlightened attitude, effective strategies can be conceived and adopted. Cooperative action is essential if we are to preserve the option of chemical disease control for our crops.

History of FRAC

FRAC and its Working Groups originated as a result of a course on fungicide resistance in 1980, and developed at an industry seminar in Brussels in 1981.

The seminar attracted 68 scientists and marketing managers from 35 major agrochemical companies worldwide. At the meeting it was apparent that there was an urgent need for collaboration. The Fungicide Resistance Action Committee was thus born as an organisation designed to discuss resistance problems and formulate plans for cooperative efforts to avoid or manage fungicide resistance. FRAC became incorporated within GIFAP, the International Group of National Associations of Manufacturers of Agrochemical Products. This organisation was later renamed Global Crop Protection Federation (GCPF). Throughout 2000 and 2001, GCPF has worked to evolve into CropLife International, the new global federation to represent the plant science industry.

Working Groups for benzimidazoles, dicarboximides, demethylation inhibitors (DMI's) and phenylamides were organised and companies were soon cooperating in monitoring studies and other technical projects. Fungicide use guidelines designed to reduce the risk of resistance developing or to manage it if it was present, were produced and have been refined as knowledge grew. The DMI Working Group was expanded to cover all Sterol Biosynthesis Inhibitors, and renamed the SBI Fungicides Working Group.

The introduction of the anilinopyrimidines in 1995 and STAR fungicides (Strobilurin Type Action and Resistance) in 1997 (now renamed QoI Fungicides Working Group) and more recently the introduction of new carboxylic acid amides (CAA fungicides) led to the formation of working groups for these new areas.

In comparison to the above-mentioned "AI-based" working groups, the Banana Working Group deals with a single crop and several chemical groups. The Banana Working Group, which was created in 2003, is comprised of banana grower associations, research institutions and chemical manufacturers. The objectives of this working group are similar to the other FRAC groups.

In 2003 the Benzimidazole, Dicarboximide and Phenylamide Working Groups were reorganized as Expert Fora. These Fora are constructed as informal networks of technical experts around the world. They provide a general global overview of the resistance situation for these groups and are updated on an "as needed" basis as new information becomes available.

Reference 6

Footnote: 21

EB1049

PLANT DISEASE

CLUB ROOT OF CABBAGE AND OTHER CRUCIFERS

Club root probably affects most plants in the crucifer (mustard) family worldwide, including cabbage, cauliflower, Brussels sprouts, broccoli, kohlrabi, kale, collards, Chinese cabbage, mustard, and some varieties of turnips, radishes, and rutabagas. Alyssum and stock are also susceptible, as are many native and weed species in the mustard family. Horseradish and winter cress are resistant. Several non-cruciferous species can be infected with club root, including members of the rose family (*Rumex* spp., e.g., sorrel and dock), poppy family (*Papaver* spp.), and grass family (*Agrostis* spp. = bentgrass, *Dactylis* spp. = orchard grass, *Holcus* spp. = velvetgrass, and *Lolium* spp. = ryegrass). However, these species rarely show typical symptoms of club root.

Causal agent

Club root is caused by the fungus *Plasmodiophora brassicae*, which produces a resting spore that can survive in the soil for 18 years or longer, as well as a motile spore (zoospore) that can "swim" in wet soils. At least 9 pathogenic types (pathotypes) of the fungus have been identified.

Symptoms

The most distinctive symptom of club root is abnormally large, distorted roots. Clubs (swellings) may form on the fine roots, secondary roots, tap root, or even the underground stem, with larger clubs (up to 5" to 6" wide) usually forming on larger roots just below the soil surface. On crops in which the fleshy root is an enlarged hypocotyl (e.g., radish, turnip, and rutabaga), clubs form on the tap root or on secondary roots and are usually globular or spherical. For hosts with more fibrous root systems (e.g., cabbage, cauliflower, and broccoli), the spindle-shaped clubs form on individual roots. Root swellings are usually not observed until about 3 weeks after infection.

If susceptible plants are infected as seedlings, they may die. However, often there are no symptoms on the top growth of seedlings, only small clubs on the roots. Club root rarely kills

Spindle-shaped clubs on the roots of a cabbage plant infected with *Plasmodiophora brassicae*.

plants infected at a later stage. Severe distortion of the roots reduces the ability of plants to absorb water and minerals, resulting in stunted top growth, yellowing of the lower leaves, and reduced yields. Infected plants may wilt during warm weather, but recover at night, and may bolt (produce a flower stem) prematurely in hot weather. Top growth may appear normal during cool, overcast conditions when the transpiration demand is low. As infection progresses, the clubs may be invaded by secondary organisms, resulting in decay of the roots and death of the plant.

Some plant species susceptible to club root (e.g., turnip, rutabaga, and rapeseed/canola) may form non-infectious hybridization nodules of an unknown cause that are easily confused with club root symptoms. Herbicide injury to the roots can also be mistaken for club root (particularly dinitroaniline herbicides such as treflan).

Disease cycle

Plasmodiophora brassicae is most active in cool, wet, acidic soils such as those found west of the Cascade Mountains. In the presence of roots of a susceptible host, resting spores of the fungus germinate to produce motile spores (zoospores) that penetrate root hairs or at wound sites on thickened roots and underground stems. Underground stems may also be infected through leaf scars. Soil moisture levels of 50 to 70% of the maximum water-holding capacity (about -20 to -15 kPa) are required for infection to occur, and club root is more severe in soils with a pH <7.0. Germination of resting spores occurs when soil temperatures reach ≥60°F.

Once a plant is infected, the fungus causes plant cells in the roots to enlarge and divide repeatedly, leading to gall (club) formation. The fungus produces masses of resting spores in these clubs. The resting spores are released into the soil when the clubs rot, and may remain viable in the soil for more than 18 years. *Plasmodiophora brassicae* is spread by movement of infested soil clinging to farm equipment, tools, and shoes. The pathogen can spread on infected transplants and in contaminated manure, irrigation water, and drainage water. Repeated production of crucifers on the same land leads to rapid buildup of the pathogen in fields.

Root system of a plant infected with club root, showing clump- or fist-like galls (clubs) which eventually rot and release resting spores of *Plasmodiophora brassicae into* the soil.

Management

Cultural control. Cultural practices play a very important role in effective long-term control of club root:

1. Purchase disease-free transplants from a reputable dealer and transplant seedlings into well-drained soils free from *P. brassicae.*
2. If producing transplants, sanitation is very important for effective control of club root. Use only non-infested seedbeds and clean transplant media, trays, and equipment. Do not lime seedbeds or transplant media heavily as this may mask symptoms of club root and symptoms could become severe after seedlings

are transplanted into soil with a lower pH.

3. Do not allow water to drain from an infested field into an irrigation source, and avoid using irrigation water contaminated with *P. brassicae.*
4. If some crops are infected and others are free from club root, work in club root-free crops before moving people and machinery into infected crops to avoid spreading infested soil to non-infested areas. Clean soil thoroughly from machinery and equipment before moving from an infested field into a clean field. Use soap and water to wash tools used to handle infected plants.
5. Control wild mustards in crucifer crops.
6. Practice long-term (6+ years) crop rotation to help prevent buildup of inoculum of *P. brassicae.*
7. Dispose of infected plants in the garbage or a dump. Do NOT put infected culled plants in a compost pile.
8. Do not use manure from animals fed infected culled plants or from animals pastured in infected crops.
9. Good soil drainage and maintenance of a high soil pH by regular application of lime help control club root. The degree of control is influenced by soil pH, and different soil types vary in their response to altering pH with lime. High concentrations of calcium and magnesium may provide control of club root when the soil pH is <7.2. Conversely, low calcium and magnesium may permit club root to develop if the soil pH is >7.2. If susceptible crops are to be planted into suspect or infested fields, incorporate limestone at least 6 weeks prior to planting to raise the soil pH >7.0. Late summer or fall applications of lime, when the soil is dry, are more effective than spring applications. Use lime that will increase both soil pH and soil calcium, i.e., calcitic lime is usually more effective than dolomitic lime unless soils are low in magnesium. Mix the hydrated lime thoroughly into the soil (1,500 lbs/acre) for maximum disease control. Finely-ground lime alters the pH more rapidly than coarse granules. Lime will not prevent development of club root if the concentration of spores of *P. brassicae* in the soil is high. Periodically monitor changes in soil pH in subsequent years to determine the stability of the pH change. Be aware that increasing the soil pH of coarse-textured soils may lead to boron deficiency, which can be alleviated with foliar applications of boron or inclusion of boron in the transplant water. In addition, some non-crucifer crops have problems with high lime content in the soil, which should be taken into consideration if a non-crucifer crop will follow the crucifer crop. For example, scab of potatoes is made worse by liming.
10. Nitrogen fertilization can affect development of club root. Fertilization with calcium nitrate may result in less disease compared with applications of ammonium sulfate or urea. Research done in Canada (by Elmhirst and Zimmerman, as reported in the 2001 Pest Management Research Report for Agriculture and Agri-Food Canada) showed that side-dressing brassica crops with calcium nitrate 3 weeks after transplanting significantly reduced root clubbing.
11. If club root develops in a crop, hilling the plants promotes production of adventitious roots which may help the infected crop yield better.
12. Cabbage cultivars with resistance to multiple lines of the club root fungus are available, e.g., "Badger Shipper" and "Richelain." Some cultivars are resistant to select races of the fungus.

Chemical control. For home gardeners, no fungicides are registered for control of club root. For commercial growers, several fungicides have shown efficacy for control of club root and can be incorporated into an effective integrated disease management program with the cultural practices described above.

1. Seedbeds can be fumigated if pathogen-free soils are not

available. Preplant soil treatment with PCNB (Terraclor 75WP or Terraclor F) does not prevent development of club root, but reduces the number of clubs formed as well as secondary root rots. PCNB can be broadcast or banded into the soil at planting, or applied in the transplant water.

2. Soil fumigation with metam sodium (e.g., Vapam or Sectagon) applied by rotovate-and-roll or spray-blade fumigation effectively controlled club root when evaluated in a cauliflower crop in western Washington.
3. Researchers in British Columbia, Canada, demonstrated that cyazofamid (Ranman) provided excellent control of club root when applied in-furrow with a surfactant. There was no evidence of phytotoxicity from cyazofamid (Elmhirst and Zimmerman, 2001 Pest Management Research Report for Agriculture and Agri-Food Canada). This product is currently not registered for this use in Washington State.
4. In Canada, application of fluazinam (Omega) in-furrow in the transplant water provided good control of club root on cauliflower in organic soils (Elmhirst and Zimmerman, 2001 Pest Management Research Report for Agriculture and Agri-Food Canada). However, fluazinam was phytotoxic to cauliflower on mineral soils. This product is currently not registered for this use in Washington State.

Follow label directions and precautions when applying any pesticide. Only use pesticides legally registered in your state for the particular crop on which you wish to make the application.

By Lindsey J. du Toit, Vegetable Seed Pathologist, WSU Northwest Washington REC, Mount Vernon, WA. Original bulletin prepared in November 1990 by Roy M. Davidson, Jr., Agricultural Research Technologist, and Ralph S. Byther, Emeritus Extension Plant Pathologist, WSU Puyallup REC, Puyallup, WA.

Issued by Washington State University Extension and the U.S. Department of Agriculture in furtherance of the Acts of May 8 and June 30, 1914. Extension programs and policies are consistent with federal and state laws and regulations on nondiscrimination regarding race, color, gender, national origin, religion, age, disability, and sexual orientation. Trade names have been used to simplify information. No endorsement is intended. Revised April 2004. Subject codes 270, 356. A. EB1049

Reference 7

Footnote: 22

Mustard Greens (*Brassica juncea*)-Clubroot

Cause The disease is caused by *Plasmodiophora brassicae*, a fungus-like microorganism that can survive in soil 18 years or more after an infected crop. It can be spread through any means that moves soil: wind and water, footwear and equipment, and in infected transplants. Soils that are cool, wet (70 to 80% water-holding capacity) and acidic favor the pathogen.

Clubroot probably affects all species of the Crucifer family, including wild mustard. The microorganism that causes clubroot occurs worldwide and also infects plants in the rose, poppy, and grass families including *Agrostis*, *Dactylis*, *Holcus*, and *Lolium* spp. However, these plants rarely show typical symptoms of the disease.

Symptoms Plants wilt in hot weather but partly recover at night. Top growth may be stunted, yellowish, and likely to prematurely bolt or to wilt in hot weather. The distinctive symptom is abnormally large roots-fine roots, secondary roots, the taproot, or even on the underground stem. Roots develop clubs (swellings) that can be 5 or 6 inches wide. The largest clubs usually are just below the soil surface on the larger roots. Affected seedlings will not show any root swellings until about 3 weeks after infection. When susceptible plants are attacked in the seedling stage, they can die. When plants are attacked at a later stage, the disease rarely kills, but roots that are severely distorted have a reduced capacity to absorb minerals and water from soil. But even with extensive root clubbing, top growth may be nearly normal, depending on environmental conditions and cultural practices.

Cultural control

- Grow susceptible plants in clubroot-free fields, which are difficult to find in the Willamette Valley of Oregon.
- Control wild mustards if they are a weed problem.
- If growing susceptible crops in suspect or infested fields, incorporate enough finely ground limestone the year before planting to raise the soil pH above 7. Use lime

applications that increase soil pH as well as level of soil calcium. Thoroughly mix lime into the soil to maximize potential disease control. Lime inhibits disease development, but will not prevent a disease outbreak if the spore load in the soil is sufficiently high. Different soil types vary considerably in their response to efforts to alter the pH with lime. Therefore, measure the initial soil pH, follow Soil Moisture Potential (SMP) test recommendations, and monitor the changes after application. Periodically monitor the pH in subsequent years to determine the stability of the change.

- If planting in a suspect or infected field, incorporating hydrated lime (1,500 lb/A) at least 6 weeks before planting, whether pH is neutral or alkaline, gives additional disease control.
- The form of nitrogen fertilizer can also influence disease. Using calcium nitrate may result in less disease compared to ammonium sulfate or urea.
- Early infection of seedlings can result in severe symptoms, so it is important to use only uninfected seedbeds and clean transplant media, trays, and equipment. Do not lime seedbeds or transplant-growing media heavily. It may mask the disease, which could flare up once seedlings are transplanted to a soil of lower pH.
- Never allow drainage water or soil from an infested field to enter an irrigation source. Spores are moved easily in irrigation water.
- Work in pathogen-free fields before moving people and machinery into infested fields. Thoroughly clean soil from machinery and equipment before moving from an infested field to a clean one.
- Long rotations (6 years or longer) help prevent a pathogen buildup and reduce disease.
- If clubroot occurs, hilling-up plants can encourage production of adventitious roots, which may result in a better yield.

Chemical control

- Preplant soil treatment with PCNB (Terraclor 75 WP or Terraclor F). PCNB does not control clubroot completely but reduces the number of clubs and secondary root rots so that the crop is nearly normal size. 12-hr reentry.
    - Broadcast: For transplant or direct-seeded fields, use 40 lb/A Terraclor 75 WP or 7.5 gal/A Terraclor F, depending on soil type. Disk or rototill the PCNB into the top 4 inches of soil. The treatment is effective for two (2) seasons if the soil is only rototilled and cultivated, not plowed.
    - Bands: For transplanted or direct-seeded fields. Although a savings in chemical may be made the first year by applying it in bands before planting and cultivating

it into the top 4 inches of soil, the second-year benefit from this application of chemical is lost.
    - Use starter solutions at 1 cup/plant at planting: PCNB at 2 lb/100 gal water of the 75 WP formulation or Terraclor F at 3 pints/100 gal water. Recommended only for commercial growers.
- Omega 500F at 6.45 fl oz/100 gal water as a transplant drench or 2.6 pt/A for soil incorporation. Product may cause plant stunting or delay and shorten harvest. Preharvest interval is 50 days. 48-hr reentry.

Pscheidt, J.W., and Ocamb, C.M. (Senior Eds.). 2013. Pacific Northwest Plant Disease Management Handbook.

Use pesticides safely!

- Wear protective clothing and safety devices as recommended on the label. Bathe or shower after each use.
- Read the pesticide label—even if you've used the pesticide before. Follow closely the instructions on the label (and any other directions you have).
- Be cautious when you apply pesticides. Know your legal responsibility as a pesticide applicator. You may be liable for injury or damage resulting from pesticide use.

Reference 8

Footnote: 23

http://www.uri.edu/ce/factsheets/prints/clubrootcrucifer.html

University of Rhode Island GreenShare Factsheets

Diseases of Crucifers: Clubroot

Clubroot is a worldwide problem of temperate climates in the production of cruciferous vegetables such as cabbage, broccoli, cauliflower, radishes, kale, brussels sprouts and turnips, as well as field crops such as mustard and rape. The disease was known as early as the 13th century in England where it was called "finger and toe" disease because of the shape of infected roots.

Symptoms:

The most striking symptom of clubroot is an abnormal enlargement of the root system, with clubs often thickest at the center, tapering spindle-like towards the ends. In radishes, clubroot causes distorted swellings on the base of the bulb and along the tap root. In severe cases, entire plantings are destroyed. Clubroot-infected plants often wilt on sunny days and permanent wilting may accompany advanced decay of infected roots. Severe stunting may be evident if infection occurs early and the disease progresses rapidly. The malformed and greatly enlarged roots are the key symptom of this disease.

Causal Organism:

Clubroot is caused by the soil-borne fungus *Plasmodiophora brassicae*, which only infects plants in the crucifer family. It infects susceptible host plants through root hairs. Once in the tissue, it stimulates abnormal growth of affected parts, resulting in a swollen club. Infection is favored by excess soil moisture and low pH, although it can occur over a wide range of conditions. Once a plant is infected, numerous resistant spores of the fungus are produced in the "clubbed" tissues. As these tissues decay, spores are released into the soil where they can remain infectious for at least 10 years. Contaminated soil moved by wind or water can serve as a source of infestation of nearby fields, causing outbreaks of disease in areas where susceptible crops are planted for the first time. Numerous races of the pathogen have been identified.

Mangement:

Clubroot is a very difficult disease to manage, and heavily infested areas may have to be abandoned for future crucifer production. Some control may be achieved with the following measures:

• A good crop rotation program, growing crucifers on the same soil no more than every third or fourth year, is essential to retard development of a large population of spores on land not already heavily infested.

• Remove weeds in the crucifer (Brassicaceae) family.

• Since clubroot is favored by a low pH, liming soil to pH 7.2 or above may be helpful. Raising soil pH too high, however, may interfere with the growth of succeeding crops other than crucifers. Calcitic lime is usually preferable to dolomitic lime, except for soils low in magnesium, where dolomitic lime is more effective. In course-textured soils, increasing the pH can result in boron deficiency. This may be alleviated by application of boron in transplant water or as a foliar spray.

• With transplanted crops, the use of pathogen-free seedbeds and uninfected plants is essential to prevent introduction of the disease.

- Application of an appropriate fungicide in transplant water prior to planting may help to reduce disease development.
- Clean and disinfect all machinery before moving it from infested to non-infested land.
- Some resistant cultivars are available. However, plant resistance has not been very useful in clubroot control because of rapid development of new races of the fungus.
- Grow your own transplants to ensure that the disease does not enter from infested areas on new plants.

Adapted from Sally A. Miller, Randall C. Rowe and Richard M. Riedel, Ohio State University Extension, 2000

Pesticides are poisonous! Read and follow all safety precautions on labels. Handle carefully and store in original containers out of reach of children, pets or livestock. Dispose of empty containers immediately, in a safe manner and place. Pesticides should never be stored with foods or in areas where people eat.

When trade names are used for identification, no product endorsement is implied, nor is discrimination intended against similar materials. Be sure that the pesticide you intend to use is registered for the state of use.

The user of this information assumes all risk for personal injury or property damage.

For more information, call the URI CE Gardening and Food Safety Hotline at 1-800-448-1011 or (401)874-2929 from outside Rhode Island; Monday-Thursday between 9 am and 2 pm.

Reference 9

Footnote: 25

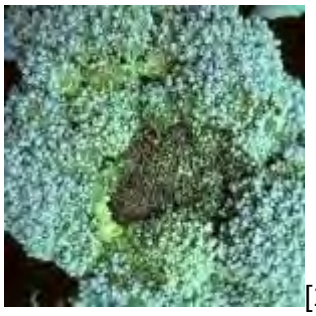
Source URL: https://extension.umass.edu/vegetable/diseases/brassica-downy-mildew

---

Brassica Downy Mildew

Halyoperonospora

parasitica

 [1]

 [2]

Downy Mildew occurs wherever brassica crops are grown and infects cabbage, Brussels sprout, cauliflower, broccoli, kale, kohlrabi, Chinese cabbage, turnip, radish, and mustard as well as cruciferous weed species. The disease caused by *Hyaloperonospora parasitica* is particularly important on seedlings but can also cause poor growth and reduced yield and quality of produce at later plant stages.

Identification:

Small, angular lesions develop on leaves and inflorescences. These lesions enlarge and become irregular, yellow to orange necrotic patches, with dense sporulation on leaf undersides. Heavy sporulation gives leaf undersides a gray to purple, downy appearance.

Life Cycle:

Downy mildew overwinters on winter-sown host crops or cruciferous weeds. Infection of leaves and inflorescences results from sporangia produced on living hosts. Secondary sporangia are spread by wind and splashing water. Oospores, if produced, survive in crop residues and in the soil. There is some evidence that *H. parasitica* may be seed borne. The pathogen is favored by cool, moist conditions.

Crop Injury:

On seedlings, cotyledons and hypocotyls may become infected and seedling loss can occur. In more mature plants, small, angular lesions develop on leaves and inflorescences. A pale brown to gray discoloration occurs on the surface of heads or curds and black streaks may develop on the stems. Affected tissues become susceptible to attack by secondary rotting organisms. Downy mildew also attacks the taproots of turnip and radish and infected organs develop a black, epidermal blotch and an internal discoloration.
Cultural Controls & Prevention:

- Removal of crop debris and weed hosts may reduce inoculum.
- Practice rotation with non-brassica crops.
- Manage Downy Mildew on transplants in the seedling bed by improving air circulation, irrigating early in the day, and applying fungicides.
- Plant resistant or tolerant cultivars.

Chemical Controls & Pesticides:
For Current information on disease recommendations ins specific crops including information on chemical control & pesticide management, please visit the New England Vegetable Management Guide website [3].

Crops that are affected by this disease:

Cabbage, Broccoli, Cauliflower, and Other Brassica Crops [4]
Radish [5]
Rutabaga and Turnip [6]

Links:

[1] https://extension.umass.edu/vegetable/sites/vegetable/files/diseases/broccoli_downey_mildew_head.jpg
[2] https://extension.umass.edu/vegetable/sites/vegetable/files/diseases/broccoli_downey_mildew_leaf.jpg
[3] http://www.nevegetable.org/
[4] https://extension.umass.edu/vegetable/crops/cabbage-broccoli-cauliflower-and-other-brassica-crops
[5] https://extension.umass.edu/vegetable/crops/radish
[6] https://extension.umass.edu/vegetable/crops/rutabaga-and-turnip

Reference 10

Footnote: 32

Phytophthora Blight: A Serious Threat to Cucurbit Industries

Mohammad Babadoost
University of Illinois
Department of Crop Sciences
AW-101 Turner Hall
1102 S. Goodwin Ave.
Urbana, IL 61801
Email: babadoos@uiuc.edu

Introduction

Phytophthora blight, caused by the oomycete *Phytophthora capsici*, has become one of the most serious threats to production of cucurbits and peppers, both in the United States and worldwide (2,6,8,9,11,17,18,22,27,30). *Phytophthora capsici* was first described by Leonian on pepper in New Mexico in 1922 (20). In 1931, Tucker (38) classified it as a species of the genus *Phytophthora* and considered *P. capsici* as a host-specific fungus pathogenic on pepper. Subsequently, taxonomists (23,36,37) studied *Phytophthora* isolates from various hosts in the world and re-described the taxonomy of *P. capsici*.

Recently, the incidence of Phytophthora blight on cucurbits has dramatically increased in Illinois (2,32) and other cucurbit-growing areas in the world (8,9,17,18), causing up to 100% yield loss. Cucurbit industries, particularly processing industries, are seriously threatened by heavy crop loss resulting from Phytophthora blight. For example, outbreaks of Phytophthora blight have threatened the processing pumpkin and other cucurbit industries in Illinois, where 90% of processing pumpkins produced in the US are grown (2,3) (Figs. 1 and 2). Similarly, the pickling cucumber industry of Michigan is jeopardized by the increased occurrence of Phytophthora blight (8). Because of heavy crop losses the growers often have to abandon their own farms for cucurbit production and move into different areas, sometimes traveling more than 50 miles, to find fields not infested with *P. capsici*.

Fig. 1. A processing pumpkin field (and pumpkins, inset) at harvest in Illinois.

Fig. 2. A cucurbit fruit showcase at a farm in Illinois.

At present, no single method provides adequate control of *P. capsici* on cucurbits. No cucurbit cultivar with measurable resistance is available. In addition, crop rotation is virtually ineffective because the pathogen can survive for several years in the soil (8,40), and it can infect more than 50 plant species, including several weed species (6,32). Research is clearly needed to develop effective strategies for the management of Phytophthora blight caused by *P. capsici* on cucurbits and other vegetables.

Geographical Distribution

Phytophthora capsici on cucurbits was first reported in 1937 in Colorado and California (15,33). Since then Phytophthora blight has been observed in cucurbit growing areas throughout the world (4,5,6,7,40). *Phytophthora capsici* infection commonly occurs in temperate, subtropical, and tropical environments.

Host Range

In 1996, Erwin and Ribeiro (6) reported that 49 plant species can be infected by *P. capsici*. Among the major hosts are red and green peppers (*Capsicum annuum*), watermelon (*Citrullum lanatus*), cantaloupe (*Cucumis melo*), honeydew melon (*C. melo*), cucumber (*Cucumis sativus*), blue Hubbard squash (*Cucurbita maxima*), acorn squash (*Cucurbita moschata*), gourd (*C. moschata*), processing pumpkin (*C. moschata*), yellow squash (*Cucurbita pepo*), (*C. pepo*), zucchini squash (*C. pepo*), tomato (*Lycopersicon esculentum*), black pepper (*Piper nigrum*), and eggplant (*Solanum melongena*). In 2004, Tian and Babadoost (32) reported five crop species/varieties -- beet (*Beta vulgaris*), Swiss chard (*Beta vulgaris* var. *cicla*), lima beans (*Phaseolus lunatus*), turnip (*Brassica rapa*), and spinach (*Spinacia olerace*) -- and one weed species, velvetleaf (*Abutilon theophrasti*), as hosts of *P. capsici* for the first time.

Symptoms and Signs

Phytophthora capsici can strike cucurbit plants at any stage of growth. The infection usually appears first in low areas of the fields where the soil remains wet for longer periods of time (Fig. 3A). The pathogen infects seedlings, vines, leaves, and fruit (Fig. 4).

Fig. 3. Post-emergence damping-off of pumpkin seedlings: (A) a low area in a pumpkin field with severe seedling death; (B) damping-off of a seedling.

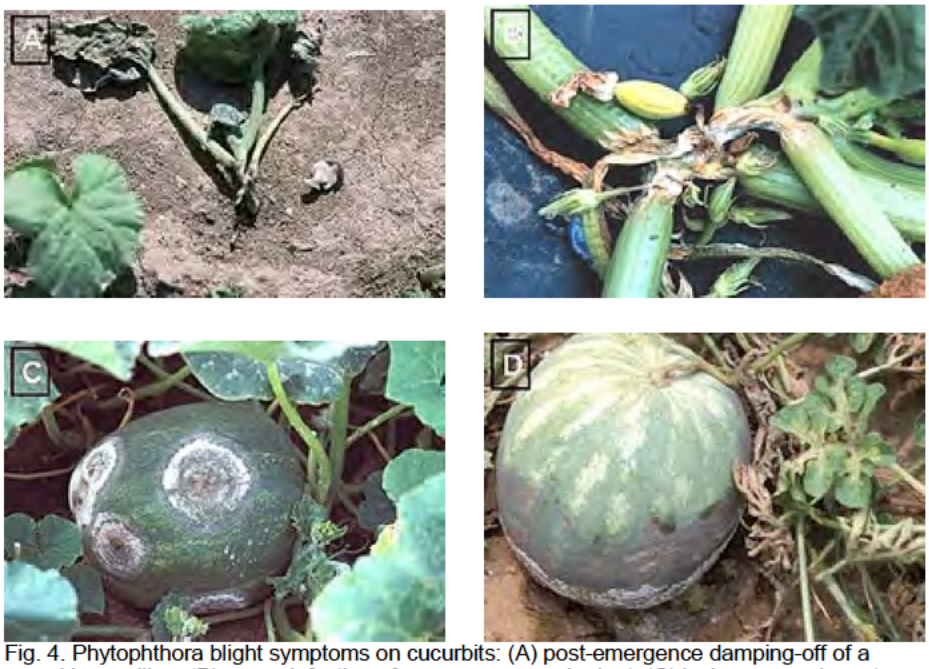


Fig. 4. Phytophthora blight symptoms on cucurbits: (A) post-emergence damping-off of a pumpkin seedling; (B) crown infection of a summer squash plant; (C) lesions on an immature processing pumpkin fruit; (D) fruit rot of watermelon.

Damping-off. *Phytophthora capsici* causes pre- and post-emergence damping-off in cucurbits in wet and warm (20 to 30°C) soil conditions (5,6,12,40) (Fig. 3). In seedlings, a watery rot develops in the hypocotyls at or near the soil line, resulting in plant death (Fig. 3B). Post-emergence seedling death is preceded by plant wilting. Mature plants show symptoms of crown rot (Fig. 4B). Initial symptoms include a sudden, permanent wilt of infected plants without a change in color (40) (Fig. 5). The wilt of leaves progresses from the base to the extremities of the vines. Often plants die within a few days of the first appearance of symptoms or after the soil is saturated by excessive rain or irrigation. The stem near the soil line turns light to dark brown and becomes soft and water-soaked. Infected stems collapse and die. Tap and lateral roots of infected processing pumpkin plants usually do not exhibit any symptoms. Following death of the foliage, roots may give rise to new vines if environmental conditions become less conducive for disease development. Phytophthora damping-off may result in partial to total loss of the crop.


Fig. 5. Wilt of a pumpkin plant as a result of crown infection with *P. capsici*.

Vine blight. Vines can be affected at any time during the growing season (2,6,40). Water-soaked lesions develop on vines (Fig. 6). The lesions are dark olive in the beginning (Fig. 6A) and become dark brown in a few days (Fig. 6B). The lesions girdle the stem, resulting in rapid collapse and death of foliage above the lesion site (Figs. 6C, 6D, and 7). Unaffected parts of the vine continue to grow if no girdling lesion develops along the vine.

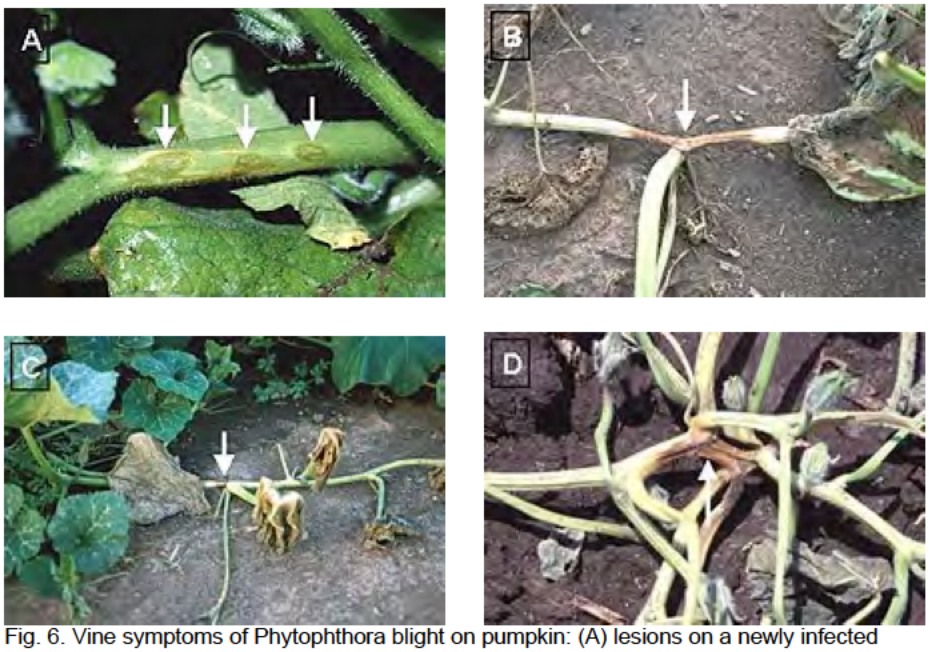


Fig. 6. Vine symptoms of Phytophthora blight on pumpkin: (A) lesions on a newly infected vine; (B) a fully-developed lesion; (C) a girdling lesion affecting a part of a vine; (D) crown infection.


Fig. 7. Death of a muskmelon plant as a result of crown infection with *P. capsici*.

Leaf symptoms. *Phytophthora capsici* can infect both the petiole and leaf blade (2,40). Dark brown, water-soaked lesions develop on petioles (similar to lesions on vines), resulting in a rapid collapse and death of leaves. Infection of the leaf blade results in development of leaf spots ranging from 5 mm to more than 5 cm in diameter (Fig. 8). Infected areas are chlorotic at first and then become necrotic with chlorotic to olive-green borders in a few days. Under wet and warm conditions, leaf spots expand rapidly, coalesce, and may cover the entire leaf. Under dry conditions, expansion of leaf spots may cease.


Fig. 8. Phytophthora spots, caused by *P. capsici*, on a pumpkin leaf. Note chlorosis and necrosis.

Fruit rot. Fruit rot can occur from the time of fruit set until harvest (2,17,40) (Figs. 9 and 10). Fruit rot generally starts on the side of the fruit that is in contact with the soil (Fig. 9B). However, when an infected leaf or vine comes in contact with a fruit, fruit rot will start at the point of contact (Fig. 9C). Also, symptoms on the upper surface of the fruit develop following rain or overhead irrigation, which provides splashing water for pathogen dispersal. Fruit rot also can develop after harvest, during transit or in storage. Fruit rot typically begins as a water-soaked lesion (Fig. 9A), which expands, eventually covering the fruit with white mold (2,17) (Figs. 9 and 10). The pathogen produces numerous sporangia on infected fruit (Figs. 9 and 10). Fruit infection progresses rapidly, resulting in complete collapse of the fruit (Figs. 9D, 10C, and 10D). Phytophthora foliar blight and fruit rot may result in total loss of the crop (2).

Fig. 9. Fruit rot of processing pumpkin caused by *P. capsici*: (A) a lesion on a fruit; (B) fruit rot developed on the side contacting the soil; (C) fruit rot as a result of falling an infected leaf on fruit; (D) severely infected and collapsed fruit.

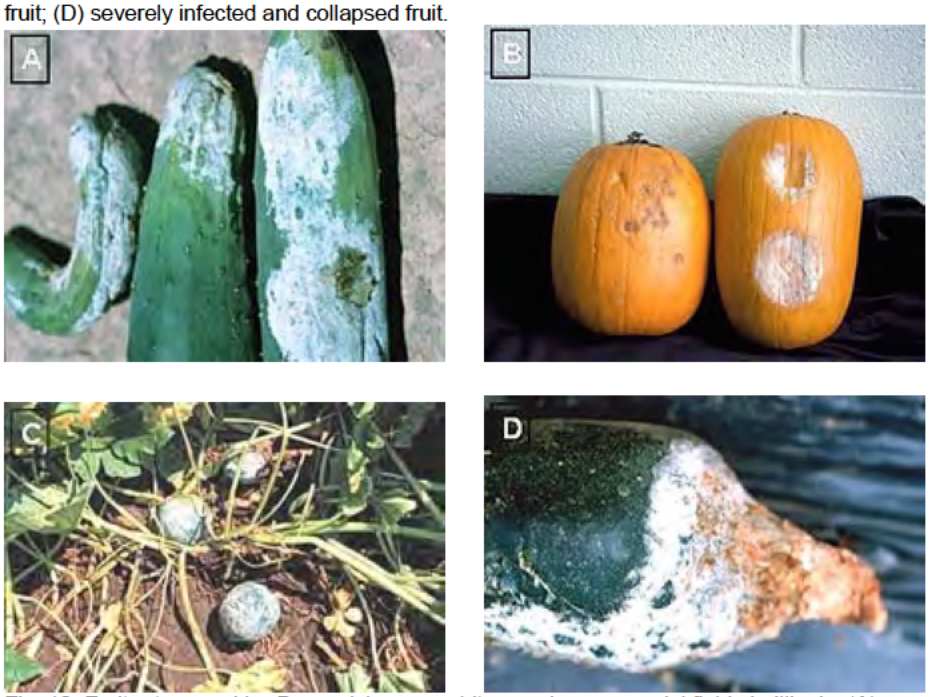


Fig. 10. Fruit rot caused by *P. capsici* on cucurbit crops in commercial fields in Illinois: (A) cucumber; (B) jack-o-lantern pumpkin; (C) acorn squash; (D) zucchini.

Pathogen Identification

Identification of *Phytophthora capsici* is mainly based on the morphology of sporangia (6). Sporangia of *P. capsici* are variable in shape and are papillate with long pedicels (Fig. 11). Sporangial shapes are influenced by light and other cultural conditions, and are subspherical, ovoid, obovoid, ellipsoid, fusiform, and pyriform. Sporangia are tapered at the base and are caducous with long pedicels. Length × width of sporangia varies from 32.8 to 65.8 × 17.4 to 38.7 µm (6). Length/breath ratios of sporangia range from 1.3:1 to 2.1:1. Pedicel lengths are highly variable among the isolates, ranging from 35 to 138 µm.

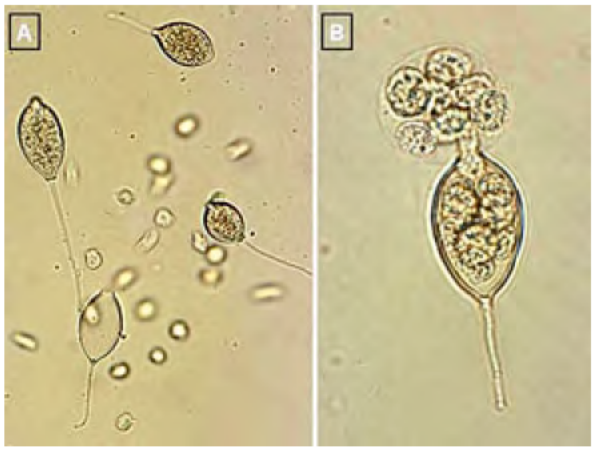


Fig. 11. Sporangia and zoospores of *P. capsici*: (A) sporangia and zoospores; (B) a sporangium releasing zoospores.

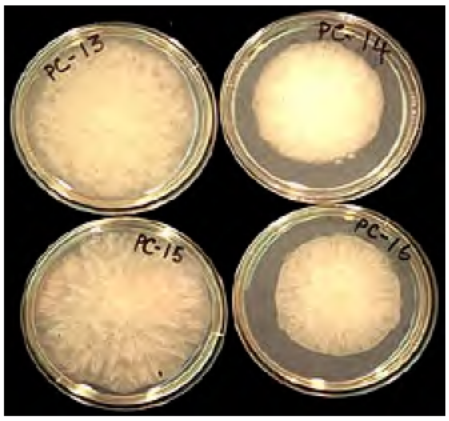


Fig. 12. Growth pattern of *P. capsici* colonies from processing pumpkin fields on lima bean agar, 5-day-old cultures.

Fig. 13. Oospores of *P. capsici*.

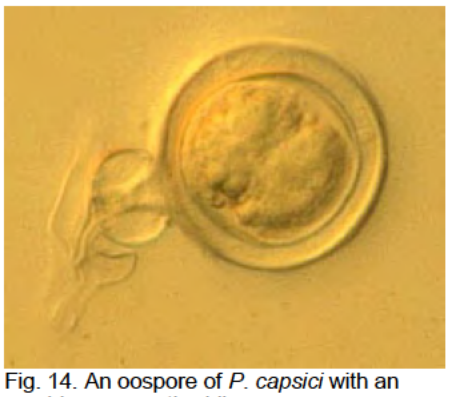


Fig. 14. An oospore of *P. capsici* with an amphigynous antheridium.

Other characteristics of *P. capsici* isolates from cucurbits are: (i) colonies grow at temperatures from 10 to 36°C, with optimum temperatures of 24 to 33°C: (ii) growth patterns of colonies are cottony, petaloid, rosaceous, and stellate (Fig. 12); (iii) oospore diameters range from 22 to 34 µm (Fig. 13); and antheridia are amphigynous (Fig. 14). *Phytophthora capsici* is heterothallic, and both A_1 and A_2 types may exist in the same field.

Pathogenic and Genetic Diversity of *P. capsici*

Cucurbit isolates of *P. capsici* have been reported to be pathogenic on cucurbits, pepper, and tomato (12,15). Polach and Wenster (25) reported distinct pathogenic strains among isolates of *P. capsici* from tomato, pepper and squash. In North Carolina, Ristaino (26) evaluated the relative virulence of isolates of *P. capsici* from cucumber and squash on pepper and found differences in virulence among the isolates. In Italy, Tamietti and Valentino (30) grouped *P. capsici* isolates into 13 classes depending on their ability to infect different plant species (pepper, tomato, eggplant, melon, squash, pea, and French bean). In South Korea, Lee, et al. (18) studied aggressiveness of *P. capsici* isolates from pepper and pumpkin on pumpkin cultivars and reported significant pathogen-host interactions. In Illinois, Tian and Babadoost (31) reported significant differences among isolates of *P. capsici* from different locations.

Genetic variation among *P. capsici* isolates has been reported in vegetable growing areas in the world (10,16,19,31). Different methods have been used to study the genetic variation of fungi (16, 21,28,34,35,39). Internal transcribed spacer (ITS) regions have been used to determine genetic differences among species of *Phytophthora* (28). Inter-simple sequence repeats (ISSR) amplification is a new technique that could rapidly differentiate closely related individuals within a fungal species (31,39). Amplified fragment-length polymorphism (AFLP) is a recently developed polymerase chain reaction (PCR) technique that provides genetic markers for fingerprinting, mapping, and studying genetic relationships among populations within fungal species (1). Tian and Babadoost (31) used ISSR and AFLP tests to determine genetic differences among isolates of *P. capsici* from Illinois (Fig. 15). They reported that cluster analysis separated the isolates into four distinct groups, representing four different locations from which they had been collected.

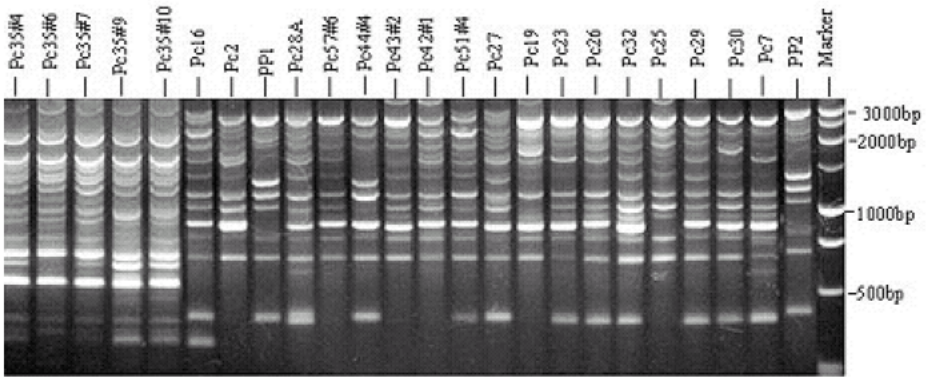


Fig. 15. Products of inter-simple sequence repeats (ISSR) test of *P. capsici* using primer (GTC)7. Marker is a 1-kb ladder (Promega, Inc. Madison, WI).

Disease Cycle and Epidemiology

Phytophthora capsici is a soilborne pathogen and survives between crops as oospores in soil or mycelium in plant debris (6,8,24,40). An oospore is a thick-walled sexual spore (Figs. 13 and 14) and is formed when mycelia of two opposite mating types (A_1 and A_2) grow together. Oospores are resistant to desiccation, cold temperatures, and other extreme environmental conditions, and can survive in the soil, in the absence of a host plant, for many years (8,40). Oospores germinate and produce sporangia and zoospores (asexual spores) (Fig. 11). Zoospores are released in water (Fig. 11B) and are dispersed by irrigation or surface water. Zoospores are able to swim for several hours and infect plant tissues. Abundant sporangia are produced on infected tissues, particularly on affected fruit (Figs. 9 and 10), and dispersed by water or through the air. Sporangia can either germinate and infect host tissues directly, or they can release zoospores, which can then infect the plant. If the environmental conditions are conducive, the disease develops very rapidly.

Soil moisture conditions are important for disease development (8,40). Sporangia form when the soil is at field capacity and they release zoospores when soil is saturated. The disease is usually associated with heavy rainfall, excessive-irrigation, or poorly drained soil. Frequent irrigation increases the incidence of the disease.

Disease Management

No single method currently available provides adequate control of Phytophthora blight. A combination of measures should be practiced to reduce the damage caused by *P. capsici* on cucurbits (2,8,12,13,14,40). The most effective practice in controlling *P. capsici* is preventing the pathogen from being moved into a new field. The following practices can help to manage Phytophthora blight in cucurbit fields:

1. Select fields with no history of Phytophthora blight.
2. Select fields that did not have cucurbit, eggplant, pepper, or tomato for at least 3 years. No rotation period has been established for effective management of Phytophthora blight of cucurbits.
3. Select fields that are well isolated from fields infested with *P. capsici*.
4. Select well-drained fields, or do not plant the crop in the areas of the field which do not drain well.
5. Clean farm equipment of soil between fields.
6. Plant non-vining crops (i.e., summer squash) on dome-shaped raised beds (approximately 25 cm high).
7. Plant resistant varieties, if available.
8. Avoid excessive irrigation.
9. Do not irrigate from a pond that contains water drained from an infested field.
10. Do not work in wet fields.
11. Scout the field for the Phytophthora symptoms, especially after major rainfall, and particularly in low areas.
12. When symptoms are localized in a small area of the field, disk the area.
13. Discard infected fruit, but not in the field.
14. Do not save seed from a field where Phytophthora blight occurred.
15. Remove healthy fruit from the infested area as soon as possible and check them routinely.

16. Do not display fruit for sale in an area that is infested with *P. capsici*.
17. Apply effective fungicides, when recommended. Seed treatment with either mefenoxam (Apron XL LS at 0.42 ml per kg of seed) or metalaxyl (Allegiance FL at 0.98 ml per kg of seed) can protects seedlings of cucurbits until 5 weeks after sowing seed (3). Applications of dimethomorph (Acrobat 50WP at 448 g/ha) plus copper sulfate (i.e., Cuprofix Disperss at 2.25 kg/ha), at weekly interwals, can provide effective protection against foliar blight and fruit rot caused by *P. capsici* in cucurbit fields (13). Crop losses resulting from Phytophthora blight in cucurbit fields can be minimized by combining Apron 50WP seed-treatment with applications of Acrobat plus copper.

Conclusion

Phytophthora blight, caused by *P. capsici*, is and will continue to be a serious threat to cucurbit production in the US and worldwide. There are no cucurbit cultivars with measurable resistance to Phytophthora blight, the pathogen survives in soils for several years, and limited chemical control of the disease is available. New strategies for management of Phytophthora blight are essential. Along with cultural management strategies, research is needed to assess the possibilities of using induced resistance in plants, genetically modified cultivars, biocontrol agents, and eradicant fungicides for control of *P. capsici* in cucurbits and other crops.

Literature Cited

1. Alonso, S., and Glenn, H. H. 1999. Modification of the AFLP protocol applied to honey bee DNA. Biotech. 26:706-709.

2. Babadoost, M. 2000. Outbreak of Phytophthora foliar blight and fruit rot in processing pumpkin fields in Illinois. Plant Dis. 84:1345.

3. Babadoost, M., and Islam, S. Z. 2003. Fungicide seed treatment effects on seedling damping-off of pumpkin caused by *Phytophthora capsici*. Plant Dis. 87:63-68.

4. C.M.I. 1985. C.M.I. description of pathogenic fungi and bacteria No. 836. *Phytophthora capsici*. CAB, Kew, England.

5. Erwin, D. C., Bartnicki-Garcia, S., and Tsao, P. H. 1995. *Phytophthora*: Its Biology, Taxonomy, and Pathology. American Phytopathological Society, St. Paul, MN.

6. Erwin, D. C., and Ribeiro, O. K. 1996. Phytophthora Diseases Worldwide. American Phytopathological Society, St. Paul, MN.

7. Farr, D. F., Bills, G. F., Chamuris, G. P., and Rossman, A. Y. 1995. Fungi on Plants and Plant Products in the United States. American Phytopathological Society, St. Paul, MN.

8. Hausbeck, M. 2004. Phytophthora lessens learned: Irrigation water and snap beans. The Vegetable Growers News 38:2829.

9. Holmes, G. J., Lancaster, M. E., Rodriguez, R. J., and Redman, R. S. 2001. Relative susceptibility of cucurbit and solanaceous drops to Phytophthora blight. Phytopathology 91:S39. Publication no. P-2001-0283-AMA.

10. Hwang, B. K., Arthur, W. A., and Heitefuss, R. 1991. Restriction fragment length polymorphisms of mitochondrial DNA among *Phytophthora capsici* isolates from pepper (*Capsicum annuum*). System. Appl. Micriobiol. 14:111-116.

11. Hwang, B. K., and Kim, C. H. 1995. Phytophthora blight of pepper and its control in Korea. Plant Dis. 79:221-227.

12. Islam, S. Z., and Babadoost, M. 2002. Effect of red-light treatment of seedlings of pepper, pumpkin, and tomato on the occurrence of Phytophthora damping-off. HortSci 37:678-681.

13. Islam, S. Z., and Babadoost, M. 2004. Evaluation of selected fungicides for control of Phytophthora blight of processing pumpkin, 2004. Fung. & Nemat. Tests 59:V129.

14. Johnston, S. A. 1982. Control of the crown rot phase of Phytophthora blight of bell pepper with fungicides. Fung. & Nemat. Tests 37:73.

15. Kreutzer, W. A., Bodine, E. W., and Durrell, L. W. 1940. Cucurbit diseases and rot of tomato fruit caused by *Phytophthora capsici*. Phytopathology 30:972-976.

16. Lamour, K. H., and Hausbeck, M. K. 2002. The Spatiotemporal genetic structure of *Phytophthora capsici* in Michigan and implications for disease management. Phytopathology 92:681-684.

17. Latin, R. X., and Rane, K. 1999. Identification and Management of Pumpkin Diseases. BP-17, Purdue University, Lafayette, IN.

18. Lee, B. K., Kim, B. S., Chang, S. W., and Hwany, B. K. 2001. Aggressiveness of isolates of *Phytophthora capsici* from pumpkin and pepper. Plant Dis. 85:797-800.

19. Lee, S. B., White, T. J., and Taylor, J. W. 1993. Detection of *Phytophthora* species by oligonucleotide hybridization to amplified ribosomal DNA spacers. Phytopathology 83:177-181.

20. Leonian, L. H. 1922. Stem and fruit blight of pepper caused by *Phytophthora capsici*. Phytopathology 12:401-408.

21. Majer, D. R., Mithen, B.G., Lewis, P. V., and Oliver, R. P. 1996. The use of AFLP fingerprinting for the detection of genetic variation in fungi. Mycol. Res. 100:1107-1111.

22. Matheron, M. E., and Matejka, J. C. 1995. Comparative activities of sodium tetrathiocarbonate and metalaxyl on *Phytophthora capsici* and root and crown rot on chile pepper. Plant Disease 79:56-59.

23. Mchau, G. R. A., and Coffey, M. D. 1995. Evidence for the existence of two distinct subpopulations in *Phytophthora capsici* and a redescription of the species. Mycol. Res. 99:89-102.

24. Papavizas, G. S., Bowers, J. H., and Johnston, S. A. 1981. Selective isolation of *Phytophthora capsici* from soils. Phytopathology 71:129-133.

25. Polach, F. J., and Wenster, R. K. 1972. Identification of strains and inheritance of pathogencity in *P. capsici*. Phytopathology 62:20-26.

26. Ristaino, J. B. 1990. Interspecific variation among isolates of *Phytophthora capsici* from pepper and cucurbit fields in North Carolina. Phytopathology 80:1253-1259.

27. Ristaino, J. B., and Johnston, S. B. 1999. Ecologically-based approaches to management of Phytophthora blight on bell pepper. Plant Dis. 83:1080-1089.

28. Ristaino, J. B., Trout, C. L., and Gregory, P. 1998. PCR amplification of ribosomal DNA for species identification in the plant pathogen genus Phytophthora. Appl. Environ. Microbiol. 64:948-954.

29. Schmitthenner, A. F., and Hilty, J. W. 1962. A modified dilution technique for obtaining single-spore isolates of fungi from contaminated material. Phytopathology 52:582-583.

30. Tamietti, G. and Valentino, D. 2001. Physiological characterization of a population of *Phytophthora capsici* Leon. from northern Italy. J. Plant Pathol. 83:1101.

31. Tian, D., and Babadoost, M. 2003. Genetic variation among isolates of *Phytophthora capsici* from Illinois. Phytopathology 93:S84. Publication no. P-2003-0613-AMA.

32. Tian, D., and Babadoost, M. 2004. Host range of *Phytophthora capsici* from pumpkin and Pathogenicity of isolates. Plant Dis. 88:485-489.

33. Tompkin, C. M., and Tucker, C. M. 1937. Phytophthora root rot of honeydew melon. J. Agric. Res. 54:933-944.

34. Tooley, P. W., Bunyard, B. A., Carras, M. M., and Hatziloukas, E. 1997. Development of PCR primers from internal transcribed spacer region II for detection of *Phytophthora* species infecting potatoes. Appl. Environ. Microbiol. 63:1467-1475.

35. Trout, C. I., Ristaino, J. B., Madritch, M., and Wangsoomboondee, T. 1997. Rapid detection of *Phytophthora infestans* in late blight infected potatoes and tomatoes using PCR. Plant Dis. 81:1042-1048.

36. Tsao, P. H. 1991. The identities, nomenclature and taxonomy of *Phytophthora* isolates from black pepper. Pages 185-211 in: Diseases of Black Pepper. Proc. Int. Pepper Comm. Workshop on Black Pepper Diseases. Goa, India. Y.R. Sarma and T. Premkumar, eds.

37. Tsao, P. H., and Alizadeh, A. 1988. Recent advances in the taxonomy and nomenclature of the so-called "*Phytophthora palmivora*" MF4 occurring on cocoa and other tropical crops. Pages 441-445 in: 10th Int. Cocoa Res. Conf. Proc. Santo Domingo.

38. Tucker, C. M. 1931. Taxonomy of the genus *Phytophthora* deBary. Univ. MO. Agric. Exp. Stn. Res. Bull. 153.

39. White, T. J., Bruns, T., Lee, S., and Taylor, J. 1990. Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. Pages 315-322 in: PCR protocols: a guide to methods and applications. M. A. Innis, D.H. Gelfand, J.J. Sninsky, and T.J. White, ed. Academic Press, Inc., New York, N.Y.

40. Zitter, T. A., Hopkins, D. L., and Thomas, C. E. 1996. Compendium of Cucurbit Diseases. American Phytopathological Society, St. Paul, MN.

Electronic Resources for Further Information

http://vegetablemdonline.ppath.cornell.edu/PhotoPages/Impt_Diseases/Cucurbit/Cuc_Phytop.htm (Phytophthora blight photos -- from Cornell's Vegetable MD Online)

http://veg-fruit.cropsci.uiuc.edu/Vegetables/Main/vegetables.htm (Vegetable diseases -- from U of Illinois' Dept. of Crop Sciences)

http://www.ces.ncsu.edu/depts/pp/notes/Vegetable/vdin027/vdin027.htm (Phytophthora Blight of Peppers and Cucurbits -- from North Carolina Cooperative Extension Service)

http://www.greeen.msu.edu/April00updates/020GREEEN1999.pdf (An Integrated Approach to Manage Phytophthora Blight on Michigan's Vine Crops -- PDF from Project GREEEN at Michigan State University)

http://digital.library.okstate.edu/oas/oas_pdf/v75/p1_5.pdf (*Phytophthora capsici* Zoospore Infection of Pepper Fruit in Various Physical Environments -- from the Oklahoma Academy of Science)

http://www.bitkisagligi.net/Cucurbit_Phytophthora_capsici.htm (*Phytophthora capsici* Kök Boðazý Çürüklüðü)

http://www.apsnet.org/online/feature/pumpkin/phyto.html (Phytophthora Fruit Rot -- from an APS*net* Feature, American Phytopathological Society)

http://www.ces.purdue.edu/extmedia/BP/BP-17/BP-17.pdf (Identification & Management of Pumpkin Diseases -- PDF from Purdue Cooperative Extension)

http://edis.ifas.ufl.edu/pdffiles/CV/CV12300.pdf (Cucurbit Production in Florida -- PDF from University of Florida's Institute of Food and Agricultural Sciences (IFAS))

http://www.cfgrower.com/tips/august/managing.html (Managing Phytophthora Blight in Cucurbit Crops -- from Country Folks Grower)

http://www.ag.uiuc.edu/~vista/abstracts/a945.html (Phytophthora Blight of Cucurbits -- from the VISTA infobase of the University of Illinois)

American Phytopathological Society
3340 Pilot Knob Road
St. Paul, MN 55121-2097
e-mail: aps@scisoc.org

Reference 11

Footnote: 33

http://www.agf.gov.bc.ca/cropprot/pcapsici.htm

Phytophthora Blight of Cucurbits and Pepper

Phytophthora blight, caused by the fungus-like pathogen *Phytophthora capsici*, was detected on pepper, pumpkin, squash, gourds and eggplant in British Columbia, for the first time in 2004. It was confirmed in two neighbouring market gardens in the Kelowna area, where it caused significant damage.

Phytophthora blight is a serious threat to production of susceptible crops worldwide, particularly cucurbits and solanaceous plants. It is a fast spreading, aggressive disease, capable of causing complete crop failures. The disease has been increasing in severity in the United States in recent years, where outbreaks have threatened the survival of the processing pumpkin industry. Many vegetable growers are familiar with a close relative of this disease - late blight of potato and tomato, caused by *Phytophthora infestans*.

Hosts

Crops that can be infected by *Phytophthora capsici* blight include pumpkin, many types of squash, gourd, watermelon, cantaloupe, honeydew melon, cucumber, peppers, eggplant and tomato. In 2004, US researchers reported that beet, Swiss chard, lima beans, turnip and spinach were also susceptible. In total, there are over 50 susceptible species, including many common weeds.

Symptoms

Infected pumpkin fruit covered with white cottony growth and sporangia of Phytophthora capsici.

Infected pumpkin fruit turned completely white by growth of Phytophthora capsici

Phytophthora capsici may affect all parts of the plant, causing a wide variety of symptoms. It may cause pre- and post-emergence damping-off, stem and vine blight, wilting or fruit rot. Symptoms can appear as fast as 3 to 4 days after initial infection when temperatures are warm.

Damping-off may occur both before and after emergence of seedlings in susceptible crops in the spring. Symptoms include a watery rot near the soil line, wilting, and subsequent plant death. White fungal growth may appear on infected areas of blighted seedlings under moist conditions. Damping-off is more likely to occur when soil conditions are wet and warm (20 to 30°C), and when the disease is well established in the soil. Many other fungi and fungus-like organisms can also cause damping-off, including *Pythium, Rhizoctonia* and *Fusarium* species. Damping-off caused by *P. capsici* has not yet been found in British Columbia. It is possible that local spring soil temperatures may not be warm enough to favour early infection.

Cucurbits

All cucurbits are susceptible to Phytophthora rot, but squash and pumpkin are the most commonly affected. Cucumber and melon are considered to be somewhat tolerant.

Foliar symptoms on leaves and petioles appear as rapidly expanding, irregular, water-soaked lesions, resulting in a rapid collapse and death of leaves. Leaf spots are chlorotic (yellow) at first and then turn brown with yellow or light green borders.

Vine blight appears as water-soaked lesions on the vines. Lesions turn brown and necrotic within a few days, resulting in stem girdling, wilting and death of foliage above the lesions. Dieback of shoot tips, wilting, shoot rot, and plant death quickly follow initial infection. *P. capsici* can devastate entire squash plantings in a matter of days when conditions are warm and moist.

Fruit rot was the predominant symptom seen on pumpkin, squash and gourds during the Kelowna outbreak in 2004. Fruit rot often starts on the underside of the fruit where it sits on the soil. It can also develop on the upper side of the fruit following rain or overhead irrigation. Early symptoms include large, water-soaked or slightly sunken, circular lesions, which expand to cover the fruit with white mold. The mold consists of millions of sporangia (spores), which can spread with wind and rain to cause further infections. The white fungal growth of *P. capsici* on the fruit should not be confused with the white growth of powdery mildew, which is a common problem on cucurbit leaves. Fruit rot progresses rapidly, resulting in complete collapse of the fruit and invasion of secondary rots. Fruit rot can also develop after harvest.

Yellow scallop squash fruit covered with white cottony growth and sporangia of Phytophthora capsici

Gourd fruit infected with Phytophthora capsici

Pepper

On pepper, infection of the stem near the soil line is common. Stem lesions start as dark, water-soaked areas which become brown to black and result in girdling, wilting and plant death. *P. capsici* may also cause root rot and foliar blight on pepper. On leaves, small, water soaked lesions expand and turn a light tan colour. White moldy growth may be seen on leaves during wet periods. Rapid blighting of leaves and shoots may occur. Pepper fruit can also be infected through the fruit

stalk. Fruit rot appears as dark green, water-soaked areas that become covered with a white to gray mold. Infected fruit dries, becomes shrunken and wrinkled, and remains attached to the stem.

Pepper plants killed by Phytophthora blight

Eggplant

Fruit rot is the most common symptom of phytophthora blight in eggplant. Symptoms appear as a round, dark brown area on the fruit, which is surrounded by a rapidly expanding lighter tan zone. Fruit lesions and eventually whole fruit may be covered with white to gray moldy growth during wet periods.

Eggplant fruit showing symptoms of Phytophthora blight infection in the field.

Infected eggplant fruit showing discolouration and light sporulation of Phytophthora capsici.

Tomato

Infection of field tomatoes was not observed in B.C. in 2004, although tomato crops were grown near infected peppers, pumpkins and squash. However *P. capsici* does cause serious problems in tomatoes in other areas.

Phytophthora blight can cause crown rot, leaf spot, foliar blight and fruit rot in tomatoes. Fruit rot begins as dark, water-soaked spots, often where fruit is touching the soil. The infected spot rapidly expands during warm weather to cover most of the fruit surface with a brown, watery discoloration that may appear as concentric rings. Under humid conditions, infected fruit may be covered with white moldy growth and rot entirely following invasion by secondary microorganisms. Similar symptoms can also be caused by the late blight pathogen, *Phytophthora infestans*.

Life Cycle

P. capsici is a soilborne pathogen which overwinters as oospores (thick-walled resting spores) in the soil or in plant debris. Oospores are resistant to desiccation and cold temperatures, and can survive in the soil for many years.

In the spring, oospores germinate to produce sporangia and zoospores (asexual spores) when soil moisture is at field capacity. Sporangia are spread by wind and water through the air and are carried with water movement in soil. Sporangia germinate to directly infect host tissue, or if conditions are wet, they can also germinate to release zoospores. Zoospores are motile and swim to invade host tissue. *P. capsici* can also be spread in infected transplants, seed, and through contaminated soil and equipment.

Abundant sporangia are produced on infected tissues, particularly on infected fruit. Sporangia are spread in water, by rainsplash, or in air currents. Wind-borne sporangia can be carried long distances. If the environmental conditions are favourable, the disease develops very rapidly.

Phytophthora blight is favoured by high soil moisture, frequent rains or irrigation, and warm temperatures (optimum 24-33 ^{o}C). The disease is usually associated with heavy rainfall, excessive-irrigation, or poorly drained soil. *P. capsici* does not survive cold temperatures very well unless oospores are present.

Pathogen variation and strains

P. capsici shows considerable genetic variation. Different pathogenic strains may have the ability to infect different crops, and there are also differences in virulence, or the ability to cause disease in host plants. Some strains may be more aggressive than others on certain hosts.

Limited pathogenicity tests were conducted at the Pacific Agri-Food Research Centre using *P. capsici* isolates collected from pumpkin and squash in Kelowna in 2004. The B.C. isolates were able to cause infection of sweet pepper, winter squash and golden zucchini, but did not infect musk melon.

P. capsici has 2 mating types, A1 and A2. When both mating types are present in the same field, the pathogen is able to reproduce sexually and produce oospores - a type of spore that can survive for many years in the soil. To date, only one mating type has been detected in B.C. from the 2004 outbreak.

Prevention

P. capsici had never been reported in British Columbia before 2004, and the 2004 outbreak was very small and localized. The disease was not detected in 2005. Some precautions can be taken to avoid introducing it to your farm.

Seed Source: The disease may have been introduced to the Kelowna area on infected seed. Use a reliable source for disease-free seed and transplants. Do not collect seed from an infected field.

Scouting: Early detection may help to avert serious losses. Scout your field regularly for disease symptoms. Pay particular attention to low areas of the field where the soil remains wet for longer periods of time.

Identification: Submit suspected *P. capsici* infected plants to the Plant Diagnostic Laboratory or contact a Ministry of Agriculture Plant Pathologist for disease diagnosis. Proper identification of pests and diseases is an important component of integrated pest management.

Biosecurity: Take precautions to prevent spreading diseases between fields, and to prevent possible introductions of diseases from fields of other growers. Be aware that *Phytophthora* may be carried on clothing, foot-ware and farm equipment. Refer to the publication: *Biosecurity Guidelines* for more information.

Disease Management

Phytophthora blight is a difficult disease to control, particularly once established in the soil as oospores. Management strategies should combine cultural and chemical controls, along with other disease prevention measures.

- Crop rotation is an excellent disease management strategy for most vegetable diseases. Rotate to non-susceptible or non-host crops for at least 2 years. Be sure there is no crop residue left from previous infected crops before replanting. Note, crop rotation is not effective in areas where oospores are present in the soil. When soil is infested, it may be best to move production of susceptible crops to a field with no history of the disease. Currently it is not known whether the disease has successfully overwintered in Okanagan soils.
- Control volunteer crop plants and susceptible weeds such as nightshade during crop rotations. Control weeds during the growing season.
- Plant resistant varieties, if available. Some pepper varieties have tolerance to Phytophthora blight. Check seed suppliers for resistance ratings. There are no cucurbit cultivars with measurable resistance currently available.
- Select well-drained fields, and avoid planting into low-lying areas. Raised beds are recommended for non-vining cucurbits.
- Do not over-irrigate. Discontinue overhead irrigation if the disease is present.
- When symptoms are localized in a small area of the field, disk the area. This will help to prevent movement of spores from infected plants to healthy plants during subsequent rainfalls.
- Clean equipment before moving it from infested to clean areas.
- Do not work in wet fields.
- Do not keep cull piles. Bury or remove infected plant material from the vicinity of fields and vegetable stands/display areas.
- Remove healthy fruit from the infested area as soon as possible and check them periodically for symptoms. Cull all fruit with symptoms, and do not leave culls on the field.
- There are no fungicides registered for control of *P. capsici* blight in Canada, and fungicides have not been highly effective in other areas. However fungicides applied for other diseases may provide some level of control, particularly fungicides that are effective against late blight or downy mildew. Preventive sprays are more effective than spray programs started after the disease symptoms are already present. For best results, the use of fungicides should always be combined with other disease management practices. Consult the Vegetable Production Guide for current fungicide recommendations.

Links for Further Information

- Phytophthora Blight: A Serious Threat to Cucurbit Industries, by Mohammad Babadoost, University of Illinois - APSnet
- Scary Diseases Haunt Pumpkins and Other Cucurbits - APSnet
- Phytophthora Blight of Cucurbits, Pepper, Tomato, and Eggplant - Thomas A. Zitter, Department of Plant Pathology, Cornell University
- Vegetable Diseases Caused by Phytophthora capsici in Florida, by P.D. Roberts, R.J. McGovern, T.A. Kucharek, and D.J. Mitchell - University of Florida
- Greenhouse and Field Evaluation of Bell Peppers for Resistance to Phytophthora Blight, by M. Babadoost, S. Z. Islam, and M. Hurt - University of Illinois

Reference 12

Footnote: 35

Plant Pathology Fact Sheet SP-159

Vegetable Diseases Caused by *Phytophthora capsici* in Florida

P.D. Roberts, R.J. McGovern, T.A. Kucharek, and D.J. Mitchell, respectively, Assistant Professor, Southwest Florida Research and Education Center, Immokalee, FL 34120 ; Associate Professor, Gulf Coast Research and Education Center, Bradenton, FL 34203, Professors, Plant Pathology Department, University of Florida, Gainesville FL 32611. Revised 2000

Florida Cooperative Extension Service/ Institute of Food and Agricultural Sciences/ University of Florida/ Christine Waddill, Dean

Introduction

Losses caused by *Phytophthora capsici* have consistently occurred in pepper production areas on the east coast of Florida for the past two decades. The disease is a sporadic problem in pepper, summer squash, and watermelon in most other vegetable production areas of the state, including most notably, southwest and west central Florida. *Phytophthora capsici* can cause also significant losses in eggplant and tomato. The pathogen has been reported to cause severe epidemics in Central and South America, Europe, Asia, and many other states in the United States. The host range of *P. capsici* is wide and, additionally includes cantaloupe, chayote, cucumber, honeydew melon, marigold, macadamia nut, papaya, and pumpkin. Diseases caused by *P. capsici* are often referred to as Phytophthora blight.

Symptoms

Phytophthora capsici causes seed rot and seedling blight in many solanaceous crops (pepper, eggplant, tomato) and cucurbits (cantaloupe, cucumber, summer squash, pumpkin, watermelon), similar to those seen with damping-off fungi and other *Phytophthora* spp. Rotting of seedlings prior to emergence (preemergence damping-off) and blighting of recently emerged seedlings (postemergence damping-off) can occur. The roots and plant base may be discolored and infected seedlings often fall over. White fungal growth may cover infected areas of blighted seedlings under moist conditions. *Phytophthora capsici*, as well as other *Phytophthora* spp., can also produce a wide variety of symptoms on mature plants that vary by host.

Pepper

Roots, stems, foliage, and fruit of mature pepper plants are susceptible. Although infection can occur at any height on stems, it is most common at the soil line, and starts as a dark, water-soaked area. Stem lesions become dark brown to black and result in girdling and plant death (Figure 1). Infected roots are dark brown and mushy. Leaf spots are at first small, irregular to round, and water-soaked. With age, the spots enlarge, turn a light tan, and may crack. Infected areas may be bordered by white fungal growth during wet periods. Rapid blighting of new leaves and the entire emerging shoot may take place (Figure 2).

Pepper fruit is infected through the fruit stalk. Fruit rot appears as dark green, water-soaked areas that become covered with a white to gray mold (Figure 3). Infected fruit dries, becomes shrunken, wrinkled, and brown, and remains attached to the stem.

Eggplant

Although the entire plant may be susceptible, fruit rot is the primary symptom caused by *P. capsici* in eggplant. It begins as a round, dark brown area on any part of the fruit at any stage of maturity. The initial lesion is surrounded by a rapidly expanding light tan region (Figure 4). White to gray fungal growth may appear during wet, humid periods, starting on the oldest part of the fruit lesion. Phytophthora fruit rot in eggplant lacks the concentric patterns and dark fruiting structures present with Phomopsis rot. Fruit rot in eggplant may also be caused by other *Phytophthora* spp.

Tomato

Phytophthora capsici can cause crown infections, leaf spot, and foliar blight in tomato transplants, which are most severe within the first four weeks after planting in the field. Diseased crowns are brown and soft and the plant may wilt and topple over. Another common symptom is fruit rot. Uninjured fruit of any age may be infected. Rot is most prevalent where fruit contacts the soil and begins as dark, water-soaked spots. The spot rapidly expands during warm weather and covers 50% or more of the fruit surface with a brown, watery discoloration that may assume the appearance of concentric rings (Figure 5). At first, infected fruit remains smooth and firm even though the discoloration extends to its center. Over time and under humid conditions infected fruit may be covered with white fungal growth and rot entirely following invasion by secondary microorganisms. The symptoms of fruit rot in tomato caused by two other *Phytophthora* spp., *P. drechslera* and *P. nicotianae*, are essentially the same. However, tomato fruit rot caused by *P. infestans* (late blight) is characterized by wrinkling and a definite, sunken margin.

Summer Squash

Summer squash is highly susceptible to Phytophthora foliar blight and fruit rot. Early foliar symptoms include rapidly expanding, irregular, water-soaked lesions in leaves. Dieback of shoot tips, wilting, shoot rot, and plant death quickly follow initial infection (Figure 6). Sunken, dark, water-soaked areas appear in infected fruit, and are rapidly covered by white fungal growth. Given optimal warm, wet weather, *P. capsici* can devastate entire squash plantings in a matter of days.

Watermelon

Watermelon foliage is less susceptible than that of summer squash to *P. capsici*; foliar symptoms of Phytophthora blight in watermelon are generally limited to water-soaked leaf blotches, which dry and turn brown, and dieback. However, a fatal crown rot can occur in watermelon plants of all ages during periods of excessive soil moisture and high pathogen pressure. Likewise, all stages of watermelon fruit are highly susceptible. Early symptoms of fruit rot include rapidly expanding, irregular, brown lesions-that become round to oval. Concentric rings within a lesion may occur. The centers of rotted areas are covered with a grayish mold, while the outer margins of lesions appear brown and water-soaked (Figure 7). The entire fruit eventually decays. Initial symptoms of bacterial fruit blotch of watermelon are similar to those caused by *P. capsici*.

However, after lesions expand, the two diseases can be easily separated because of the presence of extensive rind cracking and absence of fungal growth with bacterial fruit blotch, while Phytophthora rot is characterized by abundant fungal growth accompanied by little or no cracking.

Other Cucurbits

Phytophthora capsici causes rapid blighting and death of chayote plants and a fruit rot similar to that observed in watermelon. Angular, water-soaked lesions (Figure 8), as well as a rapid fruit rot, which is covered with white fungal growth, are produced in cucumber. Symptoms of Phytophthora blight in cantaloupe include leaf lesions and tip dieback of vines.

Disease Cycle

Phytophthora capsici may survive in and on seed and host plant debris in the soil by means of thick-walled, sexually-produced spores (oospores). Both mating types of the pathogen necessary for oospore production are present in Florida. The pathogen produces spores of another type called zoospores that are contained within sac-like structures called sporangia. Zoospores are motile and swim to invade host tissue. Plentiful surface moisture is required for this activity. The sporangia are spread by wind and water through the air and are carried with water movement in soil. *Phytophthora capsici* is also moved as hyphae (microscopic fungal strands) in infected transplants and through contaminated soil and equipment. Since water is integral to the dispersal and infection of *P. capsici*, maximum disease occurs during wet weather and in low or waterlogged parts of fields. Excessive rainfall, such as that which occurs during "El Niño" years, coupled with standing water creates ideal conditions for epidemics caused by *P. capsici*. Growth of this pathogen can occur between 7-37°C (46-99°F), but temperatures between 27-32°C (80-90°F) are optimal for producing zoospores and the infection process. Under ideal conditions, the disease can progress very rapidly and symptoms can occur 3-4 days after infection. Therefore, *P. capsici* can rapidly affect entire fields.

Management

Management practices in transplant production areas include the use of pathogen-free and fungicide-treated seed, and sterile potting media. Transplant trays, benches, seeding equipment and plant house benches and other structures should be disinfested using a sodium hypochlorite solution or other disinfestant. Steam sterilization of transplant trays may be useful. Transplant trays with infected plants should be removed immediately from production sites. Workers should disinfest their hands after contact with infected plants before resuming their duties.

Planting sites should be well drained and free of low-lying areas. Optimal water management is essential to prevent the occurrence of flooded field conditions that favor Phytophthora blight. The drainage area of the field should be kept free of weeds and volunteer crop plants, particularly those in the solanaceous and cucurbitaceous groups. A preplant fumigant should be used. Equipment should be decontaminated before moving between infested and noninfested fields. Infected fruit should be culled to prevent spread in the packinghouse and during shipment. Effective, labeled fungicides should be used preventively according to label instructions. It is essential that fungicides with different modes of action be rotated to prevent the buildup of fungicide resistance in *P. capsici*; rotating or tank-mixing a systemic with a contact fungicide is a good rule of thumb. Contact your county extension agent for currently labeled fungicides. Resistance to this disease has not been identified in cultivars currently grown in Florida.

Figure 1. Stem lesions at the soil line and root rot caused by *Phytophthora capsici* in pepper.

Figure 2. Foliar blight of pepper caused by *Phytophthora capsici*.

Figure 3. Fruit rot in pepper caused by *Phytophthora capsici*.

Figure 4. Fruit rot in eggplant caused by *Phytophthora capsici*.

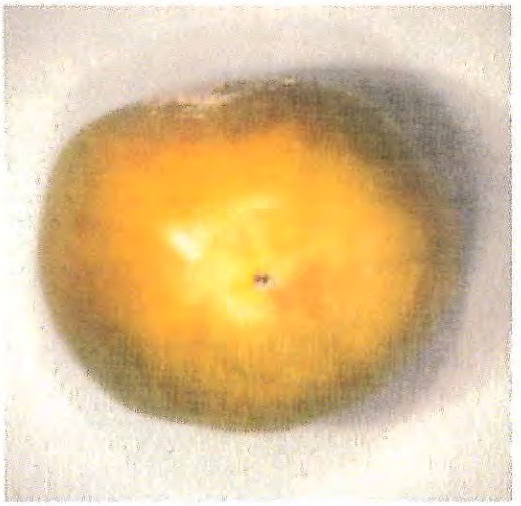


Figure 5. Fruit rot in tomato caused by *Phytophthora capsici.*

Figure 6. Foliar blight and fruit rot of yellow summer squash caused by *Phytophthora capsici.*

Figure 7. Various stages of fruit rot of watermelon caused by *Phytophthora capsici.* Left, early symptoms; right advanced symptoms.

Figure 8. Foliar lesions caused by *Phytophthora capsici* in cucumber.

Reference 13

Footnote: 36

Winter Squash Downy Mildew

Pseudoperonospora

cubensis

 [1]

Downy mildew caused by *Pseudoperonospora cubensis* is one of the most important foliar diseases of cucurbits. It occurs worldwide where conditions of temperature and humidity allow its establishment and can result in major losses to cucumber, melon, squash, pumpkin, watermelon, and other cucurbits. Downy mildew can begin to develop at any time during cucurbit crop development in the northeastern US. Fortunately it has occurred sporadically in this region, usually appearing late enough in the growing season that yield is not impacted.

Identification:

Symptoms of Downy mildew are confined to the leaves and their appearance varies widely among cucurbit species. On most species, lesions are first visible on the upper leaf surface as small, irregular to angular, slightly chlorotic areas. Symptoms appear first on older leaves and progress to younger leaves as they expand. When conditions (leaf wetness and humidity) favor sporulation, the production of fruiting bodies (sporangia) on the lower leaf surface gives the undersides of the lesions a downy appearance, varying in color from light gray to deep purple. Lesions can coalesce and result in large areas of dead tissue which exposes the fruit to sunscald. Extensive defoliation can occur when conditions are favorable.

Life Cycle:

Pseudoperonospora cubensis infects only members of the cucurbit family and is an obligate parasite. Its survival depends on the presence of cucurbit hosts, either in climates which permit their growth year round or in greenhouse culture. The source of primary inoculum in cold climates is windblown sporangia from areas where plants survive the cold season. Generally, Downy mildew of cucurbits does not arrive in southern New England until September. However, in some seasons it can move up the eastern seaboard early and arrive in July. The progress of Downy mildew is tracked by the the Cucurbit Downy Mildew Alert System (http://cdm.ipmpipe.org [2]/). Physiological specialization occurs in *P.* cubensis and at least five pathotypes have been described. Cucumber and melon are susceptible to all pathotypes, while squash and melon cultivars vary in their reactions. Spread of Downy mildew within a field can be by air currents, rain splash, workers, and tools.

Monitoring & Thresholds:

Inspect crops weekly for symptoms and have suspect samples confirmed by an extension specialist. Regularly check the UMass Vegetable website (http://extension.umass.edu/vegetable/ [3]) or Cucurbit Downy Mildew Alert System (http://cdm.ipmpipe.org [4])for information about Downy mildew occurrence, forecasts, and risks of disease development.

Cultural Controls & Prevention:

The main means of control are fungicide applications, the use of resistant cultivars, and cultural practices. Maximum control can be achieved only with a combination of these measures.

- Monitor disease occurrence and weather forecasts at http://cdm.ipmpipe.org/ [2]
- Maximize the distance between cucurbit fields to limit potential inoculum sources.
- Many commercial cultivars of cucumber have good levels of resistance to Downy Mildew. Watermelon and melon cultivars are available with low levels of resistance. Squash and pumpkin cultivars are resistant to some pathotypes but are very susceptible to compatible pathotypes. See variety tables posted at http://vegetablemdonline.ppath.cornell.edu. [5]
- Use plant spacings which reduce the density of the plant canopy. Avoid overhead irrigation. Both these practices are aimed at minimizing the length of leaf wetness periods.
- Choose planting sites with good air movement and without shading. Avoid overhead irrigation in early morning when leaves are wet from dew or late in the day when leaves will not have an opportunity to dry before dew forms.
- Apply broad-spectrum protective fungicides before detection and systemic narrow-spectrum fungicides when downy mildew occurs early in crop production.

Chemical Controls & Pesticides:

For Current information on disease recommendations ins specific crops including information on chemical control & pesticide management, please visit the New England Vegetable Management Guide website [6].

Crops that are affected by this disease:

Cucumber, Muskmelon, and Watermelon [7]

Pumpkin, Squash, and Gourds [8]

Source URL: http://extension.umass.edu/vegetable/diseases/winter-squash-downy-mildew

Links:

[1] http://extension.umass.edu/vegetable/sites/vegetable/files/diseases/winter_squash_downey_mildew_leaf.jpg

[2] http://cdm.ipmpipe.org/

[3] http://extension.umass.edu/vegetable/

[4] http://cdm.ipmpipe.org

[5] http://vegetablemdonline.ppath.cornell.edu.

[6] http://www.nevegetable.org/

[7] http://extension.umass.edu/vegetable/crops/cucumber-muskmelon-and-watermelon

[8] http://extension.umass.edu/vegetable/crops/pumpkin-squash-and-gourds

Reference 14

Footnote: 42

http://www.grapes.msu.edu/downy mildew.htm

Downy mildew - *Plasmopara viticola*

Annemiek Schilder, MSU Plant Pathology

Downy mildew is a widespread, serious disease of grapevines. Initial leaf symptoms are light green to yellow spots, called “oil spots” because they may appear greasy. Under humid conditions, white, downy spore masses can be seen on the lower leaf surface. These spores are wind dispersed. The lesions eventually turn brown as the infected tissue dies. Severely infected leaves drop prematurely, which can reduce winter hardiness of the vine. Infected flower clusters dry up or become covered with white spores under humid conditions. Infected berries turn a mottled dull-green or reddish purple and readily fall from the cluster. Although berries become resistant to infection within three weeks after bloom, the rachis remains susceptible for several weeks longer.

Young lesions.

White downy spore masses on the lower surface of the leaf.

Older lesions that have turned brown.

Photos: A. Schilder

The pathogen overwinters in infected leaves on the ground. In spring, spores are carried by rain splash to new leaves, where they require a film of water for infection. Lesions appear 5 to 17 days after infection. The disease can spread rapidly under warm conditions with frequent rain or dew. Use the 10-10-10 rule to decide when to start scouting for downy mildew: at least 10 cm (4 in.) of shoot growth, 10 mm (0.4 in.) rainfall and temperatures of 10°C (50°F) during a 24-hour period.

White spore masses develop on infected berries.

Photo: A. Schilder

On older leaves, lesions are smaller and more angular as they are delimited by leaf veins.

Photo: A. Schilder

Young shoot covered with spores. Photo: T. Zabadal

Photo: T. Zabadal

Reference 15

Footnote: 43

Downy Mildew

Downy mildew is caused by a fungus that can infect berries, leaves and young shoots. It occurs wherever it is wet and warm during the growing season. There is some variety resistance, with *V. vinifera* varieties being the most susceptible and *V. rotundifolia* being the most resistant.

Symptoms

The fungus attacks all green parts of the vine, especially the leaves. Lesions on leaves are angular, yellowish, sometimes oily, and are located between the veins. As the disease progresses, a white cottony growth can be observed on the lower leaf surface. Severely infected leaves will drop. If enough defoliation occurs, the overwintering buds will be more susceptible to winter injury. Infected shoot tips become thick, curl, and eventually turn brown and die. Young berries are highly susceptible, appearing grayish when infected. Berries become less susceptible when mature. Infected berries remain firm compared to healthy berries, which soften as they ripen. Infected berries will eventually drop.

Disease Cycle

The disease is caused by the fungus *Plasmopara viticola*, which overwinters as

dormant spores within infected leaves on the vineyard floor which become active in the spring. This fungus has two types of spores, both germinating to give rise to swimming spores. These spores swim to the stomates (breathing pores) of plants and cause infection. Water is necessary for the spores to swim and to infect, so outbreaks of the disease coincide with periods of wet weather. Downy mildew is favored by all factors that increase the moisture content of soil, air, and the plant, with rainfall being the principal factor for infection. The frequency of rain and the duration of wet periods correlate with the number of additional infections during the growing season. Downy mildew infection can become a severe problem when a wet winter is followed by a wet spring and a warm summer with a lot of rainfall.

Disease Management

Some control can be achieved by preventative management practices. Spring cultivation to bury fallen, infected leaves from the previous year may help reduce early season disease pressure. Pruning out the ends of infected shoots and practices that improve air circulation and speed drying within the vine canopy will also help to control downy mildew. Fungicides, however, are the most important control measure, especially on susceptible varieties. They should be applied just before bloom, 7 to 10 days later (usually at the end of bloom), 10 to 14 days after that, and, finally, 3 weeks after the third application. For varieties very susceptible to downy mildew, or where the disease was severe the previous season, an additional application is suggested about 2 weeks before the first blossoms open.

Reference 16

Footnotes: 46 & 50

www.agf.gov.bc.ca/cropprot/pythium.htm

British Columbia, Ministry of Agriculture

Pythium Diseases of Greenhouse Vegetable Crops

Pythium species are fungal-like organisms (Oomycetes), commonly referred to as water molds, which naturally exist in soil and water as saprophytes, feeding on organic matter. Some *Pythium* species can cause serious diseases on greenhouse vegetable crops resulting in significant crop losses. *Pythium* infection leads to damping off in seedlings and crown and root rot of mature plants. In Canada, several *Pythium* species, including *P. aphanidermatum, P. irregulare* and *P. ultimum*, are known to cause damping-off and crown and root rot in greenhouse cucumber, pepper and tomato crops. There are no *Pythium* resistant varieties available although some varieties may have disease tolerance. Over watering, poor root aeration, root injury and improper root zone temperatures can weaken the crop and, thus, trigger *Pythium* outbreaks. Saturated growing media that are either too cold or too warm can be conducive to *Pythium* build up and spread in water and recirculating nutrient solution. Plants grown under optimal environmental conditions are less susceptible to *Pythium* than plants grown under poor conditions.

Disease cycle

Pythium can be introduced into a greenhouse in plug transplants, soil, growing media, plant refuse and irrigation water. Greenhouse insects such as fungus gnats (*Bradysia impatiens*) and shore flies (*Scatella stagnalis*) can also carry *Pythium*. *Pythium* spreads by forming sporangia, sack-like structures, each releasing hundreds of swimming zoospores (Figure 1). Zoospores that reach the plant root surface encyst, germinate and colonize the root tissue by producing fine thread-like structures of hyphae, collectively called mycelium. These hyphae release hydrolytic enzymes to destroy the root tissue and absorb nutrients as a food source. *Pythium* forms oospores and chlamydospores on decaying plant roots which can survive prolonged adverse conditions in soil, greenhouse growing media and water, leading to subsequent infections.

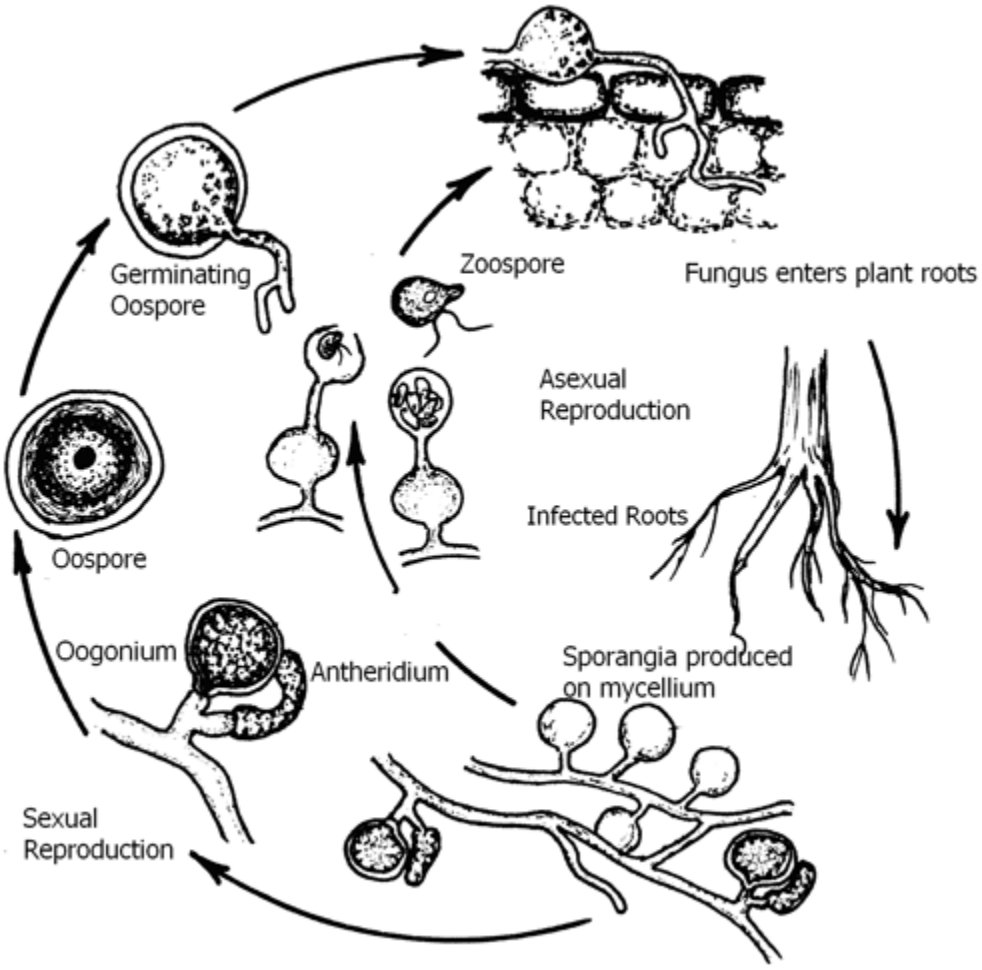


Figure 1. The disease cycle of Pythium damping-off and crown and root rot of greenhouse vegetable crops.

Symptoms

'Pre-emergence' damping-off causes seeds and young seedlings to rot before they emerge from the growing medium, while 'post-emergence' damping off kills newly emerged seedlings. In 'postemergence' damping-off, the pathogen causes a water-soaked, soft brown lesion at the stem base, near the soil line, that pinches off the stem causing the seedling to topple over and die. In mature plants, *Pythium* causes crown and root rot, where plants suddenly wilt when weather turns warm and sunny and when plants have their first heavy fruit load. Often, upper leaves of infected plants wilt in the day and recover overnight but plants eventually die. In the root system, initial symptoms appear as brown to dark-brown lesions on root tips and feeder roots and, as the disease progresses, symptoms of soft, brown stubby roots, lacking feeder roots, become visible (Figure 2). In larger roots, the outer root tissue or cortex peels away leaving the string-like vascular bundles underneath. *Pythium* rot also occurs in the crown tissue at the stem base. In cucumber, diseased crown turns orange-brown in colour, often with a soft rot at the base; brownish lesions extending 10 cm up the stem base may be seen.

Figure 2. Pythium crown and root rot in greenhouse cucumber showing orange discolouration of the crown area and rotted roots and root tips.

Monitoring & Identification

Routinely monitor your crop for slightly wilted plants and check wet areas in the greenhouse where *Pythium* is more likely to be present. *Pythium* occurs mostly in spring, at early fruit set and later in the season on mature plants. In cucumber, *Pythium* can also occur in the summer on young plants brought in for the fall crop. Monitor plants for wilting, and in cucumber, check the stem bases for discoloration. Always confirm *Pythium* diseases by sending representative plant samples with roots, crowns and foliage to a plant diagnostic laboratory or the Ministry of Agriculture's Plant Health Laboratory.

Integrated Disease Management

Disease management consists of a combination of cultural, biological and chemical tools to control and/or manage crop diseases effectively. Cultural controls keep *Pythium* from reaching the roots while biological and chemical controls inhibit or suppress *Pythium* in the root zone.

Cultural Controls

Sanitation: Field soil, debris, pond and stream water, and roots and plant refuse of previous crops can contain *Pythium*. Follow a strict greenhouse sanitation program throughout the year and a thorough year-end clean up. Clean and disinfest all interior greenhouse surfaces and equipment including tools, hoses, walkways, carts, totes,

troughs, tanks and water supply lines. Use sterile propagating media. Remove dying plants by placing them directly into plastic bags for disposal away from the greenhouse.

Irrigation water: Untreated water from rivers or streams poses great risk for *Pythium* introduction, while treated, municipal water is considered safe from *Pythium*. Water storage and nutrient tanks need to be disinfected periodically and covered to prevent *Pythium* contamination.

Nutrient Solution: Generally, greenhouse vegetables are raised on rockwool in plastic sleeves or bags containing rooting medium (i.e. rockwool slabs, sawdust or coconut fibre) through which water and nutrient solution are circulated. Since *Pythium* and other pathogens can build up in nutrient solution, periodically disinfest recirculating nutrient solution using physical, biological or chemical methods (Marchuk, 2006).

Filtration methods:
Physical - slow sand filtration, ultrafiltration (membrane filters), micro-pore filtration (high pressure, rapid flow membrane or sediment filters), heat pasteurization (95-97°C for 30 seconds or 85°C for 3 minutes), UV radiation, sonic energy, magnetism, aeration (i.e. oxygenation), ozonation, etc.
Biological - biofiltration (slow sand or lava rock), water retention ponds.
Chemical: chlorine, chlorine dioxide, copper, hydrogen peroxide, electrochemical, soaps (wetting agents), iodine, etc.

Resistant varieties: Although there are no resistant vegetable varieties, some vigorous varieties may have some tolerance to *Pythium*. Contact your local seed/transplant agent for further information on *Pythium* tolerant varieties.

Seedlings & Transplants: Transplant in the morning or late afternoon/evening to avoid stress from high day time temperatures. Allow for good air circulation around seedlings by proper plant spacing and good aeration of irrigation water and re-circulating nutrient solution. Use healthy transplants and handle them carefully to avoid wounding plants and roots and practice good sanitation when transplanting; do not let them dry when setting out. Water seedlings in the morning so that plants are not wet overnight.

Plant growing conditions: Ensure that transplants have the proper root zone temperature and adequate moisture when moved into the greenhouse. The growing media must be well drained as saturated bags with low oxygen levels can predispose transplants to *Pythium* diseases.
Use warm, aerated irrigation water (18-22°C). Avoid low light levels, low pH, high salts and warm growing conditions (above 28°C) which favour *Pythium*. In greenhouse cucumbers, the nutrient solution should be delivered at pH 5.0 for approximately 5 weeks followed by adjusting the pH to a 5.8-6.2 regime for one week. (Tu,

2004).

Target rockwool block wetness at 70-75% between watering.

Use white/colourless drip lines instead of black or place drip lines on the shaded side of the grow bags.

Disease monitoring: Plants must be monitored for any signs of *Pythium* diseases throughout the cropping cycle. Remove and destroy severely infected plants and replant in new growing bags. Infected plant materials, including grow bags, must be safely disposed away from the greenhouse by deep-burying, incinerating or composting. Control fungus gnats (*Bradysia impatiens*) and shore flies (*Scatella stagnalis*) which spread *Pythium*.

Biological and Chemical Control

Prevent *Pythium* diseases by practicing integrated disease management strategies based on cultural and biological controls. Use fungicides as a last resort at the onset of disease.

Rotate registered fungicides with different chemical groups and strictly follow label directions to avoid resistance development in *Pythium*.

Routinely monitor plants and evaluate the level of disease control if fungicides are used. Stop fungicide treatment and get professional advice if fungicides fail.

Table 1. A summary of registered fungicides and label information (Please adhere to Product label instructions when using each chemical)

Product	Chemical / biocontrol name	Chemical Group	Mode of Action	REI[1]	PHI[2]	Application
Greenhouse cucumber, pepper & tomato						
Previcur	propamocarb	28	preventative, locally-systemic	12 hrs	2 days for cucumber; 1 day for tomato & pepper	use preventatively; maximum 2 applications per crop cycle after transplanting, thereafter 7-10 days interval
Mycostop	*Streptomyces* Strain K61	biological	suppressive, non- systemic	NA	0 days	use preventatively; apply to growing medium soon after transplanting, thereafter every 3-6 weeks interval; store unopened product in a cool (≤8°C), dry place.
Prestop	*Gliocladium catenulatum*	biological	suppressive	4 hrs	0 days	use preventatively; apply to growing medium soon after transplanting, thereafter every 3-6 weeks interval;

						store unopened product in a cool (≤4°C), dry place
RootShield WP	Trichoderma harzianum Rifai, strain KRL-AG2	biological	suppressive	4 hrs	0 days	use preventatively; apply to growing medium soon after transplanting, repeat thereafter; store unopened product in a cool (2-5°C), dry place
Greenhouse cucumber						
Ridomil Gold 480EC or 480SL	metalaxyl-M, S isomers	4	preventative, systemic	12 hrs	21 days	use preventatively; one application per crop cycle; apply as drench immediately after transplanting

[1]REI - re-entry interval

[2]PHI - pre-harvest interval

NA –information is not available

For further information

1. Cherif, M. et.al. 1994. Defense responses induced by soluble silicon in cucumber roots infected by Pythium spp. Phytopathology 84: 236-242.
2. Compendium of pepper diseases. 2003. K. Pernezny, et. al. editors. The American Phytopathological Society. http://www.apsnet.org/apsstore/shopapspress/Pages/43003.aspx
3. Diseases and pests of vegetable crops in Canada. 1994. R. Howard et. al. editors. The Canadian Phytopathological Society and the Entomological Society of Canada. http://phytopath.ca/dpvcc.html
4. Growing greenhouse peppers in British Columbia. A production guide for commercial growers. 2005. BC Greenhouse Growers' Association and B.C. Ministry of Agriculture. www.bcgreenhouse.ca/publications.htm
5. Growing greenhouse vegetables. 2005. Ontario Ministry of Agriculture, Food and Rural Affairs. Publication order #371, Agdex #290. http://www.omafra.gov.on.ca/english/products/newpubs.html or products@omaf.gov.on.ca
6. Jarvis, W.R. 1992. Managing diseases in greenhouse crops. American Phytopathological Society. http://www.apsnet.org/apsstore/shopapspress/Pages/41221.aspx
7. Marchuk, R. 2006. Treatments for greenhouse recirculation water. Proceedings, 48th Annual Horticulture Growers Short Course, 2006. Lower Mainland Horticultural Improvement Association, Pages 3-8.
8. Pesticide label information for Canada: http://pr-rp.hc-sc.gc.ca/ls-re/index-eng.php
9. Tu, J. C. 2004. An integrated control measure for *Pythium* root rot of hydroponically grown greenhouse cucumbers. Acta Horticulturae 644: 571-574.
10. Zamir, P.K. and R. Yip. 2003. Biological control of damping off and root rot caused by *Pythium*

aphanidermatum on greenhouse cucumbers. Can. J. Plant Pathol. 25: 411-417.

Updated by:
Dr. Siva Sabaratnam
Plant Pathologist
Abbotsford Agriculture Centre
British Columbia Ministry of Agriculture
Iris Bitterlich

BC Greenhouse Growers' Association
May 2012

Reference 17

Footnote: 52

http://onvegetables.com/2011/05/09/white-rust-in-spinach/

Information for commercial vegetable production in Ontario

White Rust in Spinach

May 9, 2011 by Janice LeBoeuf

Marion Paibomesai, Vegetable Crops Specialist, OMAFRA

Michael Celetti, Plant Pathology Program Lead, OMAFRA

White rust (Albugo occidentalis) is a major fungal disease of spinach in the United States that occurs sporadically on spinach grown in Ontario, but when it does appear it has the potential to cause economic damage by making the spinach unmarketable. Symptoms of the disease first appear as yellow spots on the upper side of the leaf similar to downy mildew. However when the leaf is flipped over to expose the underside of the leaf, a cluster of white pustules are observed instead of a mat of grey or purplish downy growth as seen in downy mildew. Ideal conditions for white rust infection are wet and cool (16-21°C) especially when warm days are followed by cool nights with the chance of dew. This disease frequently shows up in Ontario spinach crops during August but can occur any time.

Management practices for white rust are similar to the practices used for downy mildew. There are some varieties (i.e. Regal, Samish, etc.) that are tolerant to white rust. Avoid planting fall crops in or adjacent to fields where an infected spring crop was grown and practice a 3-year crop rotation. Serenade ASO (Bacillus subtilis) is registered for suppression of white rust on spinach in Ontario; however, other products that are used to control downy mildew may also have activity on white rust. Please follow the label for precautions and directions of use.

White rust on spinach leaf

Reference 18

Footnote: 55

C. B. Skotland and Dennis A. Johnson
Irrigated Agriculture Research and Extension Center
Washington State University, Prosser

Control of Downy Mildew of Hops

The hop plant (*Humulus lupulus* L.) is a perennial with clockwise twining vine (bine) that dies back to the ground each year. The male and female flowers are borne on separate plants. The papery bracts and bracteoles of mature hop cones (Fig. 1) are used almost exclusively to flavor fermented malt beverages.

Hop downy mildew, caused by *Pseudoperonospora humuli* (Miyabe & Takah.) G. W. Wilson, is a major disease in many hop-growing areas of the world. It was first reported on wild hops in Japan in 1905 and in Wisconsin in 1909 (12). It was found in England in 1920 and 7 years later had spread throughout the hop-growing areas of Europe (12). Hop downy mildew was reported in New York State and western Washington's Puyallup Valley in 1928, in western Oregon in 1930, in California in 1934, and in the Yakima Valley of south central Washington in 1937. So far, the disease has not been found in Australia, Tasmania, New Zealand, or South Africa.

Downy mildew was a factor in the decline and loss of hop production in New York, Wisconsin, and the coastal areas of California, and its occurrence in the high-rainfall areas of western Oregon and Washington led to the demise of the cultivars Early Cluster and Late Cluster in those areas. In Oregon, the industry survived by growing the more resistant cultivar Fuggle. The susceptible Cluster cultivars were shifted to the arid regions of the Sacramento Valley of California and the Yakima and Boise valleys of the Pacific Northwest. In 1982, 82% of the United States hop acreage was concentrated in the Yakima Valley (12,150 ha), Boise Valley (1,518 ha), and Sacramento Valley (199 ha). Approximately 3,007 ha of hop are grown annually in the Willamette Valley of Oregon, where environmental conditions in the spring are conducive to mildew epidemics.

Downy mildew is a constant threat in the European hop-growing areas and is controlled by use of resistant cultivars, rigid sanitation practices, and chemicals; fungicides are often applied 8–16 times in England, Yugoslavia, and Germany (12). Epidemics occur even in the arid regions of California, Idaho, and Washington. In the Yakima Valley, the potential for an epidemic exists every year because of the extremely susceptible host and the pathogen's method of overwintering, with a serious epidemic occurring 1 year out of 3 (6).

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. § 1734 solely to indicate this fact.

Symptoms and Disease Cycle

The pathogen overwinters as mycelium in infected buds and infected crowns, and the mycelium spreads into developing buds and shoots (1,2,13). The role of oospores is not well understood, but in New York (7) they were considered important in the overwintering of the pathogen. Oospores can be readily found in infected hop tissue in most of the hop-growing areas of the world (1,7,10). In the arid areas of California, Idaho, and Washington, oospores are rare except in infected cones, where considerable numbers may be found. In the Yakima Valley, infected cones are rare even in mildew years because the dry, hot summer weather prevents spread and infected tissue rapidly becomes necrotic. In the spring, infected and healthy shoots may be growing from the same crown. Many infected crowns have only healthy shoots, while others have one to many infected shoots (Fig. 2). These infected shoots, with short internodes and yellow-green leaves that cup downward (Fig. 3), are called basal spikes and are the source of the primary inoculum. The Cluster cultivars are particularly susceptible to crown infection. Often, the crown is killed or so weakened that many shoots die before harvest.

Control Measures

Resistance. The first hop cultivars resistant to downy mildew were released in Germany in 1962 (10), but the brewing industry is reluctant to accept new cultivars. A cultivar accepted by the industry in one area may be rejected by the industry when grown in another area. Apparently, the environment affects the organoleptic properties of a cultivar in some indefinable manner when the hop cones are used directly in the brewing process. The mildew-resistant cultivars being grown in Europe are primarily the "extract" type, ie, the bittering agents are extracted from the hop cones and the extract is used. Some of these cultivars require only two or three fungicide sprays in wet environments (12). In the United States, 75% of the hops planted in arid areas are the extremely susceptible Cluster cultivars. The remaining 25% are the cultivars Bullion, Brewers Gold, and Cascade, which are tolerant to crown and foliage infection but require fungicide sprays to control foliage infection in high-rainfall areas.

Sanitation. Removing the source of primary infection effectively reduced the severity of epidemics in 1962 (14). In Idaho, weekly spike removal reduced mildew infections by 75% and enhanced control by spraying. In Washington, only 9–10% of the hills where spikes were removed weekly had spikes at the end of May, compared with 21 and 33% of the hills in yards where spikes were not removed. Romanko (9) tested various desiccant sprays for destroying the source of primary inoculum, and dinoseb (Dinitro) rapidly and almost completely eradicated infected shoots (Fig. 4). Hop vines must be trained and 2 m high before dinoseb can be applied, however, and environmental conditions during this period could favor spread of mildew.

Crown pruning. In Washington, late pruning provides some control by shortening the downy mildew season. Hops pruned early in April have considerable growth by the first of May, whereas those pruned late in April are not ready to train until mid-May. Since June weather is usually unfavorable for infection, late pruning shortens the period of potentially favorable weather from 1 month to 2 weeks. Late pruning is effective only in an environment where the downy mildew season is relatively short, however, as in the Yakima Valley.

The epidemic of 1963 in Washington provides an excellent example of the benefits of late pruning (14). Disease was severest in yards with a history of downy mildew where crowns were not pruned or

Fig. 1. Mature hop (*Humulus lupulus*) cones.

Fig. 2. Shoots growing from hop crown infected with downy mildew (*Pseudoperonospora humuli*).

Fig. 3. Infected shoots (basal spikes) with short internodes and yellow-green leaves cupping downward.

Fig. 4. Hop vines with bases sprayed with dinoseb to eradicate infected shoots.

were pruned early. By the first week of May, when weather favored infection, hops pruned early had spikes and hops pruned late did not.

Chemicals. The first recorded control measures—systematic removal of spikes and spraying with Bordeaux mixture—were in Japan in 1905. Bordeaux mixture and various copper spray materials are effective but must be coupled with sanitation practices.

Zineb has been the primary fungicide for downy mildew control in recent years. Because the ethylenebisdithiocarbamates decompose to ethylene thiourea (8), however, the brewing industry has requested that such residue be eliminated. Even though health hazards do not exist (4), the industry is concerned about possible adverse publicity. In England, zineb cannot be used within a month of harvest (12).

In Oregon, calcium cyanamide dusted over the top of the crown before shoots emerged reduced the development of basal spikes and also destroyed hop seedlings, which often are infected, presumably the result of oospore germination. Similar success was achieved in England with Bordeaux mixture and captan (2). Streptomycin sulfate reduced secondary infection and enabled shoots to recover from systemic infection in Oregon and England but has not been effective in Washington and California.

Metalaxyl has been used commercially in Europe and under emergency exemption registration during 1981–1983 in the United States. The compound has been effective in controlling downy mildew in experimental plots and growers' yards (5). The incidence of downy mildew during 1980 and 1981 in Washington ranged from 0 to 3% (percentage of hills with spikes) in replicated field plots and yards treated with metalaxyl and from 25 to 80% in adjacent plots, yards, and sections of yards not treated with metalaxyl.

Fungal resistance to metalaxyl has been reported and precautions are being taken to delay the selection and increase of resistant populations of *P. humuli*. A formulation of metalaxyl containing copper oxychloride is used in Europe as a foliar spray. For use in the United States, the manufacturer has suggested applying metalaxyl over the hop crowns before shoots emerge. When applied as a soil drench, metalaxyl is taken up by the hop roots. This application method has worked well in Oregon and during wet springs in Washington. In 1982, however, rainfall in Washington was sufficient for several infection periods but not adequate to carry the chemical into the root zones, so control was not effective.

Metalaxyl's success in controlling hop downy mildew has been outstanding in Oregon but not in Washington. The explanations for this could be that: 1) in Oregon, the cultivars are less prone to crown infection and the chemical acts on the oospores, whereas in Washington, the systemically infected shoots growing from the infected crown are the source of primary infection; 2) under the high-rainfall conditions of Oregon, metalaxyl is readily moved to the root system; 3) Oregon cultivars have a more developed root system than Washington cultivars; and 4) Washington grows more of the extremely susceptible Cluster cultivars. In Washington, spraying the foliage with metalaxyl shortly before or after training has been more effective than spraying the soil surface over the crown.

Disease prediction. Disease prediction models have been developed to strategically time fungicide applications in England, Germany, Yugoslavia, and Czechoslovakia (12). In general, these models use environmental factors, such as rain wetness duration, amount of rainfall, and relative humidity, and some include an inoculum variable to identify infection periods. Models in England (11,12) couple infection periods with the time delay of the subsequent incubation period so fungicide applications can be scheduled to protect against a second infection cycle. This does not prevent the first infection period of the season, however, which could be costly where cultivars are very susceptible to crown infection and when initial inoculum levels

are high. The model has accurately predicted infection periods and aided disease control in England (11) but missed infection periods in Washington during the 1980 and 1981 epidemics, probably because of the susceptibility of the Cluster cultivars.

A Washington model has been developed that schedules protective fungicide sprays based on the amount of initial inoculum of *P. humuli* and the likelihood of weather conditions favorable for infection. During the spring, the National Oceanic and Atmosphere Administration provides daily weather forecasts. Levels of primary inoculum are determined by visually monitoring hop yards for spikes and by monitoring environmental conditions for sporulation on spikes. Inoculum potential is estimated from the number of spikes, night temperatures, and relative humidity. Nights with temperatures higher than 5 C and relative humidity above 70% favor sporulation, whereas cool nights can delay sporangia production on spikes for several weeks. Rainy periods with temperatures above 8 C favor infection when sporangia are present.

The Washington model has had limited testing, but forecasts during the severe downy mildew epidemics in 1980 and 1981 allowed adequate scheduling of fungicide applications. Final disease incidences were 25–80% in yards where the forecasts were not followed and 0–3% in yards where they were.

Integrating the Components

Hop downy mildew exemplifies the interactions of the various components—host, pathogen, and environment—of the disease triangle. Satisfactory control in wet environments requires sanitation practices, resistant cultivars, and timely application of fungicides. In arid environments, sanitation practices and either resistant cultivars or timely application of fungicides are needed. The cultivars grown in arid environments are susceptible to crown infection, so production losses are due to crown rot and death and rarely to infected cones. The cultivars grown in wet environments are mostly resistant to crown infection, and losses result from cone infection.

In wet environments, oospores are often abundant in infected leaves, shoots, and especially cones. In dry environments, oospores are rarely found in infected leaf and stem tissue because the tissue of the very susceptible cultivars becomes necrotic, particularly when temperatures are over 30 C. The overwintering role of oospores is unclear, but in wet environments where cultivars resistant to crown infection are grown, the germinating oospore may be an important source of primary inoculum. In arid environments, *P. humuli* perennates as mycelium in crowns of susceptible cultivars, and oospores are not a means of overwintering. Control measures may reflect the overwintering method: Chemicals have been used in high-rainfall areas to prevent the development of basal spikes (3) but have not been consistently effective in arid areas on the extremely susceptible cultivars.

Literature Cited

1. Bressman, E. N., and Nichols, R. A. 1933. Germination of the oospores of *Pseudoperonospora humuli*. Phytopathology 23:485-486.
2. Coley-Smith, J. R. 1965. Infection of hop rootstocks by downy mildew *Pseudoperonospora humuli* (Miy. et Tak.) Wilson and its control by early-season dusts. Ann. Appl. Biol. 56:381-388.
3. Coley-Smith, J. R. 1966. Early-season control of hop downy mildew *Pseudoperonospora humuli* (Miy. et Tak.) Wilson with streptomycin and protectant fungicides in severely infected plantings. Ann. Appl. Biol. 57:183-191.
4. Gowers, D. S., and Gordon, C. F. 1979. Some public health aspects of the manufacture and use of zinc and manganese ethylenebisdithiocarbamate fungicides. Annu. Congr. Plant Prot. Inst. Poznan, Poland, 19th, 1979. 13 pp.
5. Hunger, R. M., and Horner, C. E. 1982. Control of hop downy mildew with systemic fungicides. Plant Dis. 66:1157-1159.
6. Johnson, D. A., Skotland, C. B., and Alldredge, J. R. 1983. Weather factors affecting downy mildew epidemics of hops in the Yakima Valley of Washington. Phytopathology 73:490-493.
7. Magie, R. O. 1942. The epidemiology and control of downy mildew on hops. Tech. Bull. N.Y. State Agric. Exp. Stn. 267:1-48.
8. Marshall, W. D. 1977. Thermal decomposition of ethylenebisdithiocarbamate fungicides to ethylenethiourea in aqueous media. J. Agric. Food Chem. 25:357-361.
9. Romanko, R. R. 1964. Control of hop downy mildew by chemical desiccants. Phytopathology 54:1439-1442.
10. Romanko, R. R., Ogawa, J. M., Skotland, C. B., Horner, C. E., and Brooks, S. N. 1964. Hop downy mildew—a symposium. Mod. Brew. Age 66:45-52.
11. Royle, D. J. 1979. Prediction of hop downy mildew to rationalize fungicide use. Pages 49-56 in: Department of Hop Research. Wye College, Annual Report for 1978.
12. Royle, D. J., and Kremheller, H. T. H. 1981. Downy mildew of the hop. Pages 395-419 in: The Downy Mildews. D. M. Spencer, ed. Academic Press, New York.
13. Skotland, C. B. Infection of hop crowns and roots by *Pseudoperonospora humuli* and its relation to crown and root rot and overwintering of the pathogen. Phytopathology 51:241-244.
14. Skotland, C. B., and Romanko, R. R. 1964. Life history of the hop downy mildew fungus. Wash. Agric. Exp. Stn. Circ. 433. 6 pp.

C. B. Skotland

Dr. Skotland is a plant pathologist with Washington State University, stationed at the Irrigated Agriculture Research and Extension Center in Prosser. He obtained his B.S. degree from Utah State University and his Ph.D. degree in 1953 from the University of Wisconsin. He investigated diseases of soybeans with the USDA at North Carolina State University, Raleigh, and has been with Washington State University since 1956. His research is on diseases of hops and mint.

Dennis A. Johnson

Dr. Johnson is extension plant pathologist and assistant plant pathologist at the Irrigated Agriculture Research and Extension Center in Prosser. After receiving his Ph.D. in plant pathology from the University of Minnesota, he was an assistant plant pathologist at the Texas Agricultural Experiment Station in Vernon. In 1980 he moved to Prosser, where he specializes in epidemiology and integrated pest management of irrigated crops.

Reference 19

Footnote: 56

Managing Downy Mildew in Hops in the Northeast

Rosalie Madden, Crop and Soils Technician & Dr. Heather Darby, UVM Extension Agronomist
Find us on the web: www.uvm.edu/extension/cropsoil/hops

Downy mildew (*Pseudoperonospora humuli*, Miyabe and Takah., Wilson) is a significant issue in hops in the Northeast. Both *Humulus lupulus* and *H. japonicas* act as a host to *P.humuli*, as do certain nettles (*Uritca* spp.) (Johnson et al. 2009). *P. humuli* is closely related to the downy mildew that you can find on familiar crops such as cucumbers and watermelons, but is not so closely related that the downy mildew from your squashes will infect your hops and vice versa (Johnson et al. 2009). Downy mildew can cause the complete loss of marketable hop yield, and even hill death in sensitive varieties (Johnson et al. 2009). It is a very serious hindrance to successful hops production, but diligent integrated pest management (IPM) can help reduce disease infection, and/or help control downy mildew once the disease has reached your hopyard. The goal of IPM practices is to integrate a multipronged approach that includes prevention, observation, and various intervention strategies to reduce or eliminate the use of pesticides, while at the same time managing pests at an acceptable level. This article will provide some guidelines and strategies on how to control downy mildew in a sustainable manner.

Disease Symptoms

One of the most critical steps in IPM is proper pest identification. Downy mildew produces characteristic diseased shoots, called "spikes" (Figures 1, 2, 4). Spikes will be stunted with short internodes, and appear chlorotic with yellow-green, down curling or cupping leaves (Johnson et al. 2009). The leaves will often be brittle, and will dry up starting at the base of the spike. In the right conditions, necrosis will eventually move to the tip of the spike. When these spikes emerge out of the crown, they are called primary basal spikes (Figure 1). On a primary spike you will see symptoms on the shoot tissue from the ground up.

Figure 1. Primary basal spike. Note short internodes, yellowing, down-curled leaves, and leaf necrosis at the base.

Figure 2. Sidearm infected with downy mildew.

Secondary spikes are diseased shoots that appear from an infected apical meristem. An apical meristem is the growing point on a plant; in the case of hops this can either be a sidearm or the top of the growing plant (Figure 2). With a secondary spike, the plant tissue below the infection remains normal in appearance, and the spike itself will usually become necrotic and desiccated in dry weather. Compared to a primary spike, the internodes may not be as noticeably

Figure 3. Downy mildew infecting the apical meristem at the top of the plant. Note how bine is falling off the string.

shortened on a secondary spike. Trained bines that become infected will often be developmentally arrested, and the bines will fall off the string (Figure 3) (Johnson et al. 2009).

Spikes are fairly characteristic of this disease, and once you see it, it is hard to mistake them for anything else. However, be forewarned that frost damage can sometimes cause symptoms similar to downy mildew (chlorosis, and, in new growth, necrosis of the leaves and shoot tips). As a result of a late frost, shoots may be stunted and older leaves may have a rough, silvery appearance (Mahaffee et al. 2009b) (Figure 4). Recent weather patterns should be taken into consideration when evaluating your hopyard early in the spring. Plants will usually recover from frost damage.

Figure 4. Frosted hops, note stunted shoots and rough, silvery leaves.

Downy mildew will cause localized leaf lesions to appear on the underside of a leaf. Downy mildew lesions are usually delimited by leaf veins, appearing angular and water soaked (Figure 5). These lesions will become necrotic and light to dark brown. Sporangia (the structure in which spores are produced) may form a mass on the underside of the leaf or spike and appear as a purple-grey or black growth (Johnson et al. 2009).

Inflorescences that become infected are dark brown, shriveled and dried up, and can fall off the plant. Cones become brown and hardened and, with an early infection, will stop developing. Depending on when the infection occurred, the cone can either be completely dark brown, or only have a few discolored bracts, giving a striped or variegated appearance (Johnson et al. 2009).

Depending on the cultivar, the appearance of infected crowns can vary. Infected crowns can appear reddish-brown to black, or have streaks in the white crown tissue next to the bark. (Be sure to not confuse the reddish-brown tissue found in the center of healthy crowns that you will find in some cultivars!) Depending on the cultivar, infected crowns can be completely rotted, appear healthy, or

Figure 3. Localized leaf lesions on surface of leaf (top) and underside of leaf (bottom). Note how lesions are delimited by leaf veins.

anywhere in between (Johnson et al. 2009).

If you would like to confirm that downy mildew has infected your hop plants, you can submit a sample to your local University Extension Plant Diagnostic Laboratory. Visit their website or call them for specifications on how to prepare and submit a sample. A diagnosis will cost between $15 and $30, depending on the lab. Contact your local Plant Diagnostic Lab by following the links below or contacting your local Extension office.

Cornell University Plant Disease Diagnostic Clinic
334 Plant Science Building
Ithaca, NY 14853

UMass Plant Diagnostic Lab
101 University Drive, Suite A7
Amherst, MA 01002

University of Vermont Plant Diagnostic Clinic
201 Jeffords Building
63 Carrigan Drive
University of Vermont
Burlington, VT 05405

Downy Mildew Lifecycle

Understanding a pest's lifecycle is important when developing a management plan. In order for a disease outbreak to occur there must be a "disease triangle", consisting of a susceptible host, a conducive environment, and the pathogen.

Like most mildews, *P. humuli* will thrive in warm, moist environments. Sporangia are usually produced when the average relative humidity is greater than 71%, and the nightly minimum temperature is greater than 41°F. The number of hours with a relative humidity greater than 80% is the greatest predictor of a downy mildew outbreak. Plant tissue needs to be moist for spores to germinate. For shoot infection to occur, water needs to be sitting for three hours with temperatures ranging from 66° –73°F or for six hours at temperatures of 46°–50°F. Leaf infection doesn't require as long of a wetness period, and can occur in 1.5–2 hours, optimally at 59°–84°F, but will occur at temperatures as low as 41°F when the leaf is wet for greater than 24 hours. A general rule of thumb is that appreciable leaf and shoot infection will occur if it is wet at moderate temperatures for four to eight hours (Johnson et al. 2009).

Downy mildew can live on infected leaves, shoots, and cones, and will usually overwinter in infected dormant buds and crowns as intercellular mycelium. Mycelium that overwinters in the crown will spread into developing buds during winter and early spring, which is why shoots are already infected when dormancy breaks, resulting in primary basal spikes. However, infected crowns don't always yield basal spikes; sometimes infected crowns will yield both healthy shoots and infected basal spikes, and sometimes infected crowns will only yield healthy shoots (Johnson et al. 2009).

Sporangia are produced on the underside of leaves at night when the temperature and humidity are favorable. These spores are released in mid-morning to early afternoon, especially in rainy conditions.

Sporangia land and germinate, producing spores that enter the plant through open stomata. The spores can infect leaves, bud stipules, apical meristems, and cones if the conditions are favorable. As discussed, infected leaves will result in localized leaf spots (Figure 5), which produce secondary inoculum to further infect more shoots, leaves, and cones. Leaf lesions usually desiccate quickly in dry weather and don't last long. Apical meristem infections, however, become systemic, producing secondary spikes and more sporangia. With an apical meristem or a secondary spike infection, the mycelium will progress down the shoot tissue toward the crown during the growing season. If the mycelium reaches the crown, hill death can result, either immediately or over time, depending on the variety. The infected plant will often die as a result of reduced carbohydrate reserves caused by the disease (Johnson et al. 2009).

Strategies for Controlling Downy Mildew

The pathogen can appear in your yard through various means. Spores can be swept in on the wind, brought in on diseased root stock, or through the grower accidently carrying it into his or her field on their clothes after visiting another hop-growing friend. Planting disease-free hop plugs is one way to be certain that you are not bringing disease into your hopyard. The Northeast Hop Alliance has started a program to propagate disease-free stock for members. Various other commercial sources can be found for disease-free stock as well. Scouting for disease should be conducted on a regular basis (weekly) to determine the degree of infection as well as to evaluate if the pathogen is spreading further. In addition, monitoring the weather conditions will help to determine if the environment is right for disease infection. Control options can be both preventative and remediative in nature. A multifaceted approach should be used to have the best success.

Cultural/Mechanical Control

Planting resistant cultivars is the first important step in preventing a serious outbreak of downy mildew (Table 1). Cultivars vary in susceptibility to crown rot and to cone, leaf, and shoot infection, but no cultivars are immune. Cascade, Fuggle, Perle, Tettnang, and Willamette all display moderate resistance to downy mildew. Cluster, Galena, Hallertauer Mittelfrüh, Hersbrucker Spält, and Nugget are all susceptible to foliar infection (Johnson et al. 2009). Bullion, Brewer's Gold, and Cascade are considered by Skotland and Johnson (1983) to be tolerant to crown and foliage infection, while still requiring fungicides to control foliage infection. Crown rot susceptibility varies among cultivars, with Cluster being extremely susceptible, which is the reason that Cluster is usually not grown in high-rainfall areas (Johnson et al. 2009).

Strict sanitation is another important step in reducing the incidence of downy mildew in your yard. Heavily diseased plants should be completely removed early in the season. Primary basal spikes should be eliminated, either mechanically or chemically (Johnson et al. 2009). Spring pruning is usually done in the late winter or early spring. The goal is to remove buds, shoots, and the previous season's bines. Various levels of aggressiveness are often employed to do this. Pruning removes all shoots prior to training. Crowning removes the top 0.75-2 inches of the crown prior to bud break. Scratching scratches the soil surface, removing buds from the top 0.75-2 inches (Beatson et al. 2009). Removing the source of

Variety	Usage	Disease Susceptibility[a]		
		Powdery Mildew	Downy Mildew	Verticillium Wilt
Brewers Gold	Bittering	S	MR	MR
Bullion	Bittering	S	MR	R
Cascade	Aroma	MR	MR	MR
Centennial	Bittering	MR	S	U
Chinook	Bittering	MS	MR	R
Columbia	Aroma	MS	MR	S
Comet	Bittering	R	S	R
Crystal	Aroma	R	S	R
East Kent Golding	Aroma	S	S	MR
First Gold	Bittering	R	S	MR
Fuggle	Aroma	MS	R	S
Galena	Bittering	S	S	R
Glacier	Aroma	S	S	U
Hall. Gold	Aroma	MS	R	S
Hall. Magnum	Bittering	S	R	MR
Hall. Mittelfrüh	Aroma	MS	S	S
Hall. Tradition	Aroma	MR	R	MR
Horizon	Bittering	MS	S	MR
Late Cluster	Aroma	S	S	R
Liberty	Aroma	MR	MR	U
Mt. Hood	Aroma	MS	S	S
Newport	Bittering	R	R	U
Northern Brewer	Bittering	S	S	R
Nugget	Bittering	R	S	S
Olympic	Bittering	S	MS	R
Perle	Aroma	S	R	MR
Pioneer	Bittering	MR	MR	U
Saazer	Aroma	S	MS	S
Saazer 36	Aroma	S	MS	S
Spalter	Aroma	S	R	MR
Sterling	Aroma	MS	MR	U
Teamaker	Aroma	MR	MR	S
Tettnanger	Aroma	MS	MS	S
Tolhurst	Aroma	S	S	U
U.S. Tettnanger	Aroma	MS	MS	S
Vanguard	Aroma	S	S	U
Willamette	Aroma	MS	MR	S

[a] Disease susceptibility ratings are based on greenhouse and field observations in experimental plots and commercial yards in the Pacific Northwest as of 2009. Disease reactions may vary depending on the strain of the pathogen present in some locations, environmental conditions, and other factors, and should be considered approximate. S = susceptible; MS = moderately susceptible; MR = moderately resistant; R = resistant; U= unknown

Table 1. Disease susceptibility and chemical characteristics of major hop varieties. Reproduced from Field Guide for Integrated Pest Management in Hops, a Cooperative Publication Produced by Oregon State University, University of Idaho, U.S. Department of Agriculture - Agricultural Research Service, and Washington State University, 2009.

primary infection can effectively reduce the severity of the epidemic (Skotland and Johnson 1983). Skotland and Johnson (1983) advise removing basal spikes weekly as it reduces mildew infection by 75%, and enhances the efficacy of spray controls. In Washington, only 9-10% of hills where spikes were removed weekly had spikes at the end of May. Where basal spikes were not removed with the same tenacity, 21-33% of hills displayed signs of infection (Skotland and Johnson 1983). Another option is to prune later in the season, which can reduce the severity of an infection, particularly in areas with shorter growing seasons. However, if pruning is done too late in the season, it will reduce yields (Johnson et al. 2009), and some argue that it may not be overly effective in a damper climate (Skotland and Johnson 1983). Beatson et al. (2009) state that pruning timing is cultivar-specific, as it affects the training timing, which in turn impacts yield. Growers will often hill up around the crown in mid-season as it encourages the development of roots and rhizomes near the top of the crown. This helps to suppress downy mildew in the current season since the diseased shoots next to the crown are buried (Beatson et al. 2009).

After training, bines should be stripped. Stripping removes the superfluous growth of leaves and laterals from the lower five feet of the trained bine (Beatson et al. 2009). Stripping reduces inoculum density, and limits the disease's spread into the upper canopy (Beatson et al. 2009; Johnson et al. 2009). Stripping also reduces the humidity around the base of the plant by increasing airflow. Stripping can be done either manually or chemically (Beatson et al. 2009). A desiccant spray can be used to simultaneously take out basal spikes and strip, but bines must be trained and at least seven feet tall before a chemical desiccant can be used without hurting the crop, and at this point it is often too late to prevent serious infection (Skotland and Johnson 1983). The date and frequency of stripping can have a significant effect on the carbohydrate reserves in the plant's root system. When you are stripping, it is important to think of what will happen three months down the road at harvest. When the bine is harvested, there needs to be enough leaf tissue left in the field so that the plant can continue to photosynthesize and accumulate carbohydrates before winter dormancy. The deleterious effects of excessive stripping can be more severe in early-maturing varieties, or plants that are already weakened by soil-borne disease (Beatson et al. 2009).

Figure 4. Hops that have been stripped to 5', and all untrained shoots and basal spikes removed.

The success of your sanitation practices depends on your thoroughness, and can help delay an epidemic. Aside from pruning and stripping, there are other practices that are critical to disease management, such as avoiding excessive nitrogen fertilization. Using overhead irrigation should also be avoided, as it increases leaf wetness. In cases with high disease incidence, an early harvest can be a tool to reduce cone infection (Beatson et al. 2009; Johnson et al. 2009).

Chemical Control

When the weather conditions are favorable for downy mildew, spraying preventatively is key (Johnson et al. 2009). Disease prediction models exist for downy mildew and hops in the Pacific Northwest and in Europe. There are currently no disease prediction models for hops in the Northeast, but the Network for Environment and Weather Applications has grape forecasting models in our region for grape downy mildew, which will give you an idea of what to expect. Use your judgment in evaluating weather patterns to determine when inoculum levels might be high. Based on the temperature and weather, it may not be necessary to spray in the early spring if it is cool, below 41°F, or if there is low relative humidity. However, low temperatures don't prevent sporulation for extended periods. Rainy weather will help liberate the sporangia from spikes (Johnson and Skotland 1985), and it is still very important to keep on top of spike removal.

When using a fungicide, be sure to read the fungicide label in its entirety! It is illegal to use a chemical on a crop or on a pest for which it is not specifically labeled, and it can often do more harm than good. Keep in mind that not all chemicals are legal in every state; be sure to check with your local Extension or Agency of Agriculture. It is also important to remember that while a chemical may be legal and labeled for use in a state there is no assurance that the material is effective against a particular pest on a particular crop, even if it is on the label. Also be sure to adhere to pre-harvest intervals and use proper personal protection equipment. Downy mildew can develop resistance to fungicides fairly rapidly; it is very important to vary the mode of action of the fungicides that you use in your yard (Johnson et al. 2009). Each class should only be used a few times per season, which is usually specified on the label. If the label permits, it can be very beneficial to tank mix fungicides that have a high risk for resistance development with fungicides that have a low risk (Mahaffee et al. 2009a). Be sure to read the label carefully, as some mixtures are phytotoxic to some crops but not others. For example, using both oil and copper products in an apple orchard will result in phytotoxicity, but will work fine with tomatoes. It is always advisable to try out a new fungicide or tank mix on a few plants to evaluate a crop's reaction before spraying the whole yard. Also note that there are some varietal differences in reactions to certain pesticides. The burr is very susceptible to mechanical damage during pesticide applications, so if at all possible, try to avoid spraying during burr development. Instead spray a product that is a very effective protectant with a long residual just prior to flowering. Basal growth should also be removed just prior to flowering to minimize the spread of disease (Mahaffee et al. 2009a).

See Table 2 for a list of approved fungicides on hops in MA, NY and VT for 2012. This list is not exhaustive; please check with your local Extension or Agency of Agriculture.

Table 2. Approved fungicides on hops in, MA, NY, and VT for 2012.

Trade Name	EPA Reg. No.	Active ingredient	Group	Protectant	Systemic	Curative	OMRI approved	Target pest					Registered		
								Powdery mildew	Downy mildew	Mites	Aphids	Other	MA	NY	VT
Actinovate AG	73314-1	*Streptomyces lydicus* WYEC 108		X		X	Y	X	X					X	X
Badge SC	80289-3	copper oxychloride, copper hydroxide		X					X				X	X	X
Basic Copper 50W HB	42750-168	basic copper sulfate	M1	X			Y		X					X	
Biocover UL	34704-806	petroleum oil	NC					X		X			X	X	
Bonide Liquid Copper Fungicide Concentrate	67702-2-4	liquid copper	M	X				X	X			X	X	X	X
Bonide Liquid Copper Fungicide Ready to Use	67702-1-4	liquid copper	M	X				X	X			X			X
Carbon Defense	84846-1	potassium silicate	M	X				X		X	X	X		X	
Champ DP Dry Prill (Agtrol)	55146-57	copper hydroxide	M	X					X				X	X	X
Champ Formula 2 Flowable (Agtrol)	55146-64	copper hydroxide	M	X					X				X	X	X
Champ WG	55146-1	copper hydroxide	M	X			Y		X					X	X
Champion Wettable Powder (Agtrol)	55146-1	copper hydroxide	M	X					X					X	X
C-O-C-S WDG	34704-326	copper oxychloride, basic copper sulfate	M1	X					X				X	X	X
Cueva Fungicide Concentrate	67702-2-70051	copper octanoate		X			Y	X	X			X	X	X	X
Cuprofix Ultra 40 Disperss	4581-413-82695	basic copper sulfate	M1	X					X					X	
Cuprofix Ultra 40 Disperss	70506-201	basic copper sulfate	M1	X					X				X	X	X
Drexel Damoil	19713-123	petroleum oil	NC					X		X			X	X	X
DuPont Kocide 101	352-681	copper hydroxide	M	X					X				X	X	X
DuPont Kocide 2000	352-656	copper hydroxide	M	X					X				X	X	X
DuPont Kocide 3000	352-662	copper hydroxide	M	X					X				X	X	X
DuPont Kocide 4.5LF	352-684	copper hydroxide	M	X					X				X	X	X
DuPont Kocide DF	352-688	copper hydroxide	M	X					X				X	X	X
Ecomate Armicarb "0"	5905-541	potassium bicarbonate	NC			X		X	X			X	X	X	X
Flint Fungicide	264-777	trifloxystrobin	11	X		X		X	X				X	X	X
Fosphite Fungicide	68573-2	phosphorous acid mono- and di-potassium salts	33	X		X		X	X			X	X	X	X
Fungi-phite	83472-1	phosphorous acid mono- and di-potassium salts	33	X		X			X					X	X
Glacial Spray Fluid	34704-849	white mineral oil		X			Y	X		X			X	X	X
JMS Stylet Oil	65564-1	paraffinic oil	NC					X		X			X	X	X
JMS Stylet Oil, Organic	65564-1	paraffinic oil	NC				Y	X		X			X	X	X
Kaligreen	11581-2	potassium bicarbonate	NC	X			Y	X					X		X
Kentan DF	80289-2	copper hydroxide	M	X					X				X	X	X
Kphite 7LP Systemic Fungicide Bactericide (Ag Label)	73806-1	phosphorous acid mono- and di-potassium salts	33	X		X		X	X				X	X	X
Kumulus DF	51036-352-66330	sulfur	NC	X			Y	X					X	X	X
MilStop Broad Spectrum Foliar Fungicide	70870-1-68539	potassium bicarbonate	NC	X				X					X	X	X
Monsoon	34704-900	tebuconazole	3	X	X			X					X		X
Nordox 75 WG	48142-4	cuprous oxide		X			Y		X					X	
Nu-Cop 3L	42750-75	copper hydroxide	M	X					X				X	X	X
Nu-Cop 50DF	45002-4	cupric hydroxide	M	X					X				X	X	X
Nu-Cop 50WP	45002-7	copper hydroxide	M	X			Y		X				X	X	X
Nu-Cop HB	42750-132	cupric hydroxide	M	X					X				X	X	
Nutrol	70644-1	potassium dihydrogen phosphate		X				X					X	X	X
Omni Oil 6E	5905-368	mineral oil		X				X		X			X	X	X
Omni Supreme Spray	5905-368	mineral oil		X				X		X			X	X	X
Prev-AM Ultra	72662-3	sodium tetraborohydrate decahydrate						X		X				X	
Pristine Fungicide	7969-199	boscalid, pyraclostrobin	7,11	X				X	X				X	X	X
Procure 480SC	400-518	triflumizole	3	X		X		X	X				X	X	X
Purespray 10E	69526-5	petroleum oil	NC					X		X			X	X	X
Purespray Green	69526-9	petroleum oil	NC				Y	X		X			X	X	X
Quintec	62719-375	quinoxyfen	13	X				X					X	X	X
Rally 40WSP	62719-410	myclobutanil	3	X	X	X		X					X	X	X
Rampart	34704-924	phosphorous acid mono- and di-potassium salts	33	X		X		X	X				X	X	X
Regalia	84059-3	extract of *Reynoutria sachalinenis*		X			Y	X	X				X	X	X
Saf-T-Side	48813-1	petroleum oil	NC	?		?	Y	X		X	X	X	X	X	
Serenade ASO	69592-12	QST 713 strain *Bacillus subtilis*		X			Y	X					X	X	X
Serenade Max	69592-11	QST 713 strain of dried *Bacillus subtilis*		X			Y	X					X	X	X
Sil-Matrix	82100-1	potassium silicate	M	X				X		X	X	X		X	
Sonata	69592-13	*Bacillus pumilus* strain QST 2808		X			Y	X	X				X	X	X
Tebuzol 3.6F	70506-114	tebuconazole	3	X	X			X					X	X	X
Trilogy	70051-2	clarified hydrophobic extract of neem oil	NC	X			Y	X					X	X	

References

Beatson, R.A., S.T. Kenny, S.J. Pethybridge, D. H. Gent. 2009. Hop Production. In W. Mahaffee, S. J. Pethybridge, & D. H. Gent (Eds.), *Compendium of Hop Diseases and Pests* (pp. 5-8). St. Paul, Minnesota: The American Phytopathological Society.

Gent, D., J.D. Barbour, A.J. Dreves, D.G. James, R. Parker, D.B. Walsh, eds. 2009. Field Guide for Integrated Pest Management in Hops. Washington Hop Commission.

Johnson, D.A. & C.B. Skotland (1985). Effects of Temperature and Relative Humidity on Sporangium Production of *Pseudoperonospora humuli* on Hop. *Ecology and Epidemiology*, *75* (2), *127-129.*

Johnson, D.A., B. Engelhard, and D.H. Gent. 2009. Downy Mildew. In W. Mahaffee, S. J. Pethybridge, & D. H. Gent (Eds.), *Compendium of Hop Diseases and Pests* (pp. 18-22). St. Paul, Minnesota: The American Phytopathological Society.

Mahaffee, W., B. Engelhard, D.H. Gent, & G.G. Grove. 2009a. Powdery Mildew. In W. Mahaffee, S. J. Pethybridge, & D. H. Gent (Eds.), Compendium of Hop Diseases and Pests (pp. 25-31). St. Paul, Minnesota: The American Phytopathological Society.

Mahaffee, W., S.J. Pethybridge, D.H. Gent. 2009b. Injuries Caused by Environmental Factors. In W. Mahaffee, S. J. Pethybridge, & D. H. Gent (Eds.), *Compendium of Hop Diseases and Pests* (pp. 73-74). St. Paul, Minnesota: The American Phytopathological Society.

Skotland, C.B. and D.A. Johnson. Control of Downy Mildew of Hops. *Plant Disease, 67, 1183-1185.*

Reference 20

Footnote: 57

http://www.cals.uidaho.edu/pses/Research/r_ent_hoppest_downymildew.htm

Hop Downy Mildew

Description and life history

Hop downy mildew is caused by the organism Pseudoperonospora humuli, a fungus related to the causal agents of hop black root and potato late blight. Like the powdery mildew fungus, hop downy mildew is an obligate parasite and can live and reproduce only in living host tissue. Cultivated hop, Humulus lupulus is its only host. Even the closely related annual or Japanese hop, H. japonicus, appears immune.

The fungus overwinters either as bud infections or as a systemically infected crown. In the spring, infected shoots, called primary spikes, emerge from the crown. Primary spikes are stunted, pale-green to yellow, upright, and brittle with downward cupped leaves.

Under cool, moist, conditions, the stem and lower leaf surfaces may bear masses of gray to black spores. These spores (zoosporangia) detach in response to mechanical agitation, raindrop splashes, and changes in relative humidity, and may be borne by the wind or by water droplets to healthy hop tissues. In the presence of free water, zoosporangia germinate releasing zoospores that swim until they reach a leaf pore (stomata), where they encyst and develop a germ tube that grows within the leaf and initiates an infection. The infection process, from zoosporangial germination to infection of the internal leaf cells, requires 2 to 3 hours at 70F. Zoosprangia will die within two days if environmental conditions do not favor germination.

Sporangia landing on buds may initiate systemic infection of axillary or terminal buds. These infected buds may in turn produce secondary spikes, which look much like primary spikes but, arise from healthy vines instead of infected crowns and usually are borne higher on the plant. Secondary infections are uncommon in the normally hot, dry climate in southern Idaho.

Damage to Hop

Losses due to downy mildew occur at several points in the disease cycle. Crown infections can result in crown rot and plant death. Bud infections do not cause plant death, but do contribute to poor plant vigor. Vine infections reduce vine vigor and may spike the growing point necessitating retraining and increasing labor costs. Flower and cone infections directly reduce marketable yield, but are uncommon in the hop growing area of southern Idaho. (back to top)

Downy Mildew Management

Downy mildew thrives in environments with moderate temperatures, high humidity, and frequent precipitation. Whenever possible, resistant varieties should be planted in fields known to have conditions favoring disease development. Cultural practices that increase air movement, decreases relative humidity, and increases summer temperatures will also help control downy mildew. When conditions favoring disease development prevail, cultural practices and plant resistance may fail to provide adequate control. Under these conditions chemical fungicides are available for downy mildew control.

APPENDICES

Appendix 1: ISKBC Latest EPA Stamped Label (9/14/12) (EPA Reg. No. 71512-3)

Appendix 2: FMC Current Supplemental Label (EPA Reg. No. 71512-3-279)

Appendix 3: USDA NASS Information for Cyazofamid Labeled Crops

Appendix 1

ISKBC Latest EPA Stamped Label (9/14/12) (EPA Reg. No. 71512-3)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL, SAFETY
AND POLLUTION PREVENTION

Mike Peplowski
ISK Biosciences Corporation
7470 Auburn Rd, Suite A
Concord, OH 44077

SEP 1 4 2012

Subject: Addition of New Uses to Ranman 400SC and Supplemental Labeling for use on Basil
EPA Registration No. 71512-3
Decision No. 456370
Submission Date: 10/11/11

Dear Mr. Peplowski:

The master label referred to above, submitted under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, to add the following uses: bean, succulent; bean, succulent, shelled; leafy greens, subgroup 4A; basil, fresh and dried leaves; vegetable, tuberous and corm, subgroup 1C; and vegetable, fruiting, group 8-10, is acceptable.

The supplemental labeling referred to above, submitted under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, with directions for use on Basil, is acceptable, provided you make the following changes:

1. At the top of the page, add the following statement, "This supplemental label expires on 9/12/15 and must not be used or distributed after this date."

2. Revise the marketing statement, "For control of diseases on basil," to read, "For control of listed diseases on basil."

3. Revise the warranty section to be identical to the master label.

A stamped copy of the master and supplemental labeling is enclosed for your records. Please submit one (1) final printed copy for the above mentioned master label before releasing the product for shipment. If you have any questions, please contact Dominic Schuler at (703) 347-0260 or via email at schuler.dominic@epa.gov.

Sincerely,

Tony Kish
Product Manager 22
Fungicide Branch
Registration Division (7504P)

ISK BIOSCIENCES

ACCEPTED
with COMMENTS
In EPA Letter Dated
SEP 1 4 2012
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 71512-3

RANMAN® 400SC

Supplemental Labeling

SUPPLEMENTAL DIRECTIONS FOR THE USE OF

Ranman 400SC
(EPA Reg. No. 71512-3)

FOR CONTROL OF DISEASES ON BASIL

Directions for Use:
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

CROP: BASIL	
DISEASE	**RATE PER ACRE**
Downy mildew *Peronospora belbahrii*	2.75 to 3.0 fl oz (0.071 to 0.078 lb a.i./A)

APPLICATION DIRECTIONS

Resistance Management:
DO NOT apply more than 9 applications of RANMAN per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC.

Application Instructions:
For control of downy mildew on basil make the applications on a 7- to 10-day schedule beginning when disease conditions are favorable for disease development. Use the lower rate and longest interval as disease preventative sprays or when disease conditions are low. Increase to the highest rate and shortest interval under moderate to heavy disease pressure. RANMAN 400SC can be applied on basil grown in a greenhouse.

RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 50 to 75 gallons per acre.

RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions following this section.

Restrictions:
DO NOT apply more than 27 fluid ounces (0.7 lb a.i.) per acre per crop growing season.
The Pre-Harvest Interval (PHI) for this crop is 0-day.
Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

NOTE: Follow all applicable directions, restrictions, and precautions on the **Ranman 400SC** label.
NOTE: This labeling must be in the possession of the user at the time of pesticide application.

ISK Biosciences Corporation
7470 Auburn Rd., Suite A
Concord, Ohio 44057

FIRST AID	
If on skin	• Take off contaminated clothing. • Rinse skin immediately with plenty of soap and water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice.
Have the product container or label with you when calling a poison control center or doctor, or going for treatment.	

HOT LINE NUMBER

For **24-Hour Medical Emergency Assistance** (Human or Animal) Call **1-888-484-7546**.

For **Chemical Emergency**, Spill, Leak, Fire or Accident, Call **CHEMTREC 1-800-424-9300**.

GROUP	21	FUNGICIDE

ISK BIOSCIENCES

RANMAN® 400SC

AGRICULTURAL FUNGICIDE

ACTIVE INGREDIENT: Cyazofamid*	34.5%
OTHER INGREDIENTS:	65.5%
Total	100.0%

*4-chloro-2-cyano-*N,N*-dimethyl-5-(4-methylphenyl)-1*H*-imidazole-1-sulfonamide (CA)

Contains 3.33 pounds Cyazofamid Per Gallon (400 grams per liter)

KEEP OUT OF REACH OF CHILDREN

CAUTION

See side panel for additional precautionary statements.

Read entire label carefully and use only as directed.

ISK Biosciences Corporation
7470 Auburn Road, Suite A
Concord, Ohio 44077 U.S.A.

EPA Reg. No. 71512-3 EPA Est. No.

Active Ingredient Made in Germany
Formulated in France

Net Contents: 2.5 Gallons

ACCEPTED

SEP 1 4 2012

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 71512-3

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS
CAUTION

Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Avoid breathing spray mist. DO NOT take internally.

Personal Protective Equipment (PPE)
Applicators and other handlers must wear long-sleeved shirt and long pants, socks, shoes, and chemical resistant gloves made of any waterproof material.

Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing. Do not allow contact of contaminated clothing with unprotected skin. Follow manufacturer's instructions for cleaning/ maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Control Statements
When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240 (d) (4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

IMPORTANT: When reduced PPE is worn because a closed system is being used, handlers must be provided all PPE specified above for "applicators and other handlers" and have such PPE immediately available for use in an emergency, such as a spill or equipment break-down.

User Safety Recommendations
Users should:
* Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.
* Remove and wash contaminated clothing before reuse.

ENVIRONMENTAL HAZARDS

DO NOT apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. DO NOT contaminate waters when disposing of equipment wash waters or rinsate.

AVOIDING SPRAY DRIFT AT THE APPLICATION SITE IS THE RESPONSIBILITY OF THE APPLICATOR. The interaction of many equipment-and-weather-related factors determine the potential for spray drift. The applicator is responsible for considering all these factors when making decisions. Where states have more stringent regulations, they must be observed.

STORAGE AND DISPOSAL

DO NOT contaminate water, food or feed by storage or disposal. Open dumping is prohibited.

PESTICIDE STORAGE: Store in original container, in a secured, dry place separate from fertilizer, food, and feed.

PESTICIDE DISPOSAL: Pesticide wastes are toxic. Improper disposal of excess pesticide, pesticide spray or rinsate is a violation of Federal law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.

CONTAINER DISPOSAL: Nonrefillable container. DO NOT reuse or refill this container. Triple rinse container (or equivalent) promptly after emptying. Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank and drain for 10 seconds after the flow begins to drip. Fill the container ¼ full with water and recap. Shake for 10 seconds. Pour rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Drain for 10 seconds after the flow begins to drip. Repeat this procedure two more times. Then offer for recycling if available, or puncture and dispose of in a sanitary landfill, or by incineration or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

FAILURE TO FOLLOW THE USE DIRECTIONS AND PRECAUTIONS ON THIS LABEL MAY RESULT IN PLANT INJURY OR POOR DISEASE CONTROL.

Do not use for disease control on fruiting vegetables (other than tomato transplants) or cucurbit vegetables grown for fruit production in greenhouses.

ROTATIONAL CROP RESTRICTIONS

Crops on this label may be planted immediately after the last treatment. Do

not plant other crops not registered for this product within 30 days after the last application.

DO NOT apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR Part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted-entry interval. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

DO NOT enter or allow worker entry into treated areas during the restricted entry interval (REI) of twelve (12) hours.

PPE required for early entry to the treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: coveralls, chemical resistant gloves made of any waterproof material, shoes plus socks and protective eyewear.

GENERAL INFORMATION

MIXING AND SPRAYING

RANMAN 400SC can be used effectively in dilute or concentrate sprays. Thorough, uniform coverage is essential for disease control.

NOTE: Slowly invert container several times to assure uniform mixture of formulation before adding this product to the spray tank.

Dosage rates on this label indicate fluid ounces of RANMAN 400SC per acre, unless otherwise stated. Under conditions favorable for disease development, the highest rate specified and shortest application interval should be used. For best product performance in all applications utilizing water volumes up to 60 gallons per acre, an organosilicone surfactant should be added according to the manufacturer's label recommendations in order to improve spray coverage when the disease infection is severe. However, a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant may be used according to the manufacturer's label when disease infection is moderate or light. Do not use a surfactant in applications to grapes or tomato greenhouse transplant production.

RANMAN 400SC may be applied with all types of spray equipment normally used for ground and aerial applications.

The required amount of RANMAN 400SC should be added slowly into the spray tank during filling. With concentrate sprays, pre-mix the required amount of RANMAN 400SC in a clean container and add to the spray tank as it is being filled. Keep agitator running when filling spray tank and during spray operations. DO NOT allow spray mixture to stand overnight or for prolonged periods. Prepare only the amount of spray required for immediate use. Spraying equipment should be thoroughly cleaned immediately after the application.

Apply RANMAN 400SC in sufficient water to obtain adequate coverage of the foliage. Gallonage to be used will vary with crop and amount of plant growth. Spray volume will usually range from 20 to 100 gallons per acre (200 to 1000 liters per hectare) for dilute sprays, and 5 to 10 gallons per acre (50 to 100 liters per hectare) for concentrate ground and aerial sprays. For aerial applications, apply RANMAN 400SC in a minimum of 5 gallons of water per acre. Application through sprinkler irrigation systems is not recommended unless specific directions are given for a crop. See application and calibration instruction below.

TANK MIX COMPATIBILITY

RANMAN 400SC is physically compatible (no nozzle or screen blockage) with many products recommended for control of diseases and insects on vegetable crops. Read and follow all manufacturer's label recommendations for the tank mix companion product. It is the applicator's responsibility to ensure that the companion product is EPA approved for use on the intended crop. RANMAN 400SC is generally compatible with other insecticides, fungicides, fertilizers and micronutrient products provided sufficient free water is available for dispersion of all the tank mix products. However, the physical compatibility of RANMAN 400SC with tank mix partners must be

evaluated before use. Conduct a jar test with intended tank-mix pesticides prior to preparation of large volumes. Use the following procedure: 1) Pour the recommended proportions of the products into a suitable container of water, 2) Mix thoroughly and 3) Allow to stand 5 minutes. If the combination remains mixed or can be re-mixed readily, it is considered physically compatible. Any physical incompatibility in the jar test indicates that RANMAN 400SC should not be used in the tank-mix.

RANMAN 400SC is physically compatible (no nozzle or screen blockage) with the following list of products:

Product	Active Ingredient
Acrobat	**dimethomorph**
Applaud	**buprofezin**
BT (several)	**Bacillus thuringiensis**
Chlorothalonil (several)	**chlorothalonil**
Curzate	**cymoxanil**
Decis	**deltamethrin**
EDBC (several)	**mancozeb**
Guthion	**azinphos-methyl**
Headline /Cabrio	**pyraclostrobin**
Karate	**lambda-cyhalothrin**
Lannate	**methomyl**
Mineral oils	
Monitor / Tamaron	**methamidophos**
Omega	**fluazinam**
Previcur	**Propamocarb hydrochloride**
Provado	**imidacloprid**
Quadris /Abound	**azoxystrobin**
Thiodan	**endosulfan**
Trigard	**cyromazine**

CROP RESPONSE

RANMAN 400SC is not phytotoxic to the crop or succeeding crops when applied according to label instructions.

INTEGRATED PEST MANAGEMENT

RANMAN 400SC is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. Although RANMAN 400SC has limited systemic activity, it should be utilized as a protectant fungicide and applied before the disease infects the crop. Depending upon the level of disease pressure, good protection of the crop against disease can be expected over a period of 7 to 10 days. RANMAN 400SC is recommended for use as part of an Integrated Pest Management (IPM) program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage. Practices known to reduce disease development should be followed. Consult your state cooperative extension service or local agricultural authorities for additional IPM strategies established in your area. RANMAN 400SC may be used in State Agricultural Extension advisory (disease forecasting) programs that recommend application timing based upon environmental factors that favor disease development.

RESISTANCE MANAGEMENT

Some plant pathogens are known to develop resistance to products used repeatedly for disease control. RANMAN 400SC's mode/target site of action is complex III of fungal respiration: ubiquinone reductase, Qi site, FRAC code 21. A disease management program that includes alternation or tank mixes between RANMAN 400SC and other labeled fungicides that have a different mode of action and/or control pathogens not controlled by RANMAN 400SC is essential to prevent disease resistant pathogens populations from developing. RANMAN 400SC should not be utilized continuously nor tank mixed with fungicides that have shown to have developed fungal resistance to the target disease.

Since pathogens differ in their potential to develop resistance to fungicides, follow the directions outlined in the "Directions For Use" section of this label for specific resistance management strategies for each crop. Consult with your Federal or State Cooperative Extension

Service representatives for guidance on the proper use of RANMAN 400SC in programs that seek to minimize the occurrence of disease resistance. RANMAN 400SC is not cross-resistant with other classes of fungicides that have different modes of action.

DIRECTIONS FOR USE			
Crop	**Diseases**	**Use Rate Fl. Oz. Product Per Acre (lb. ai/A)**	**Instructions**
Basil	Downy mildew (*Peronospora belbahrii*)	2.75 to 3.0 (0.071 to 0.078)	**Resistance Management:** DO NOT apply more than 9 applications of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions:** For control of downy mildew on basil, make the applications on a 7- to 10-day schedule beginning when disease conditions are favorable for disease development. Use the lower rate and longest interval as disease preventative sprays or when disease conditions are low. Increase to the highest rate and shortest interval under moderate to heavy disease pressure. RANMAN 400SC can be applied on basil grown in a greenhouse. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 50 to 75 gallons per acre. RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 27 fluid ounces (0.7 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
BRASSICA (COLE) LEAFY VEGETABLES: CROP GROUP 5 **Broccoli; Chinese broccoli (gai lon); broccoli raab (rapini); Brussels sprouts; cabbage; Chinese cabbage (bok choy); Chinese cabbage (napa); Chinese mustard (gai choy); cauliflower; cavalo broccolo; collards; kale; kohlrabi; mizuna; mustard greens; mustard spinach; rape greens; turnip greens**	**Club root (Plasmodiophora brassicae)** Downy mildew (*Peronospora parasitica*)	**Transplant Soil Drench:** 12.9 to 25.75 (0.333 to 0.665 per 100 gallons **Soil Incorporation:** 20 / A (0.52) **Foliar:** 2.75 / A (0.072)	**Resistance Management:** DO NOT apply more than six (1 soil + 5 foliar) applications of RANMAN 400SC per crop. Alternate foliar sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions:** **Transplant Soil Drench for control of club root:** Immediately after transplanting, make a single application within the rate range listed and apply 1.7 fluid ounces of solution per plant as transplant water. Use the lowest rate for fields with low soil infestation and increase to the higher rates when fields have a history of moderate to high soil infestation. **Soil Incorporation:** Alternatively, if desired and for soil with low infiltration rates, apply 20 fl oz per acre in a minimum bandwidth of 9 inches along the planting row and incorporate to a soil depth of 6 to 8 inches with a precision incorporator in the same operation. Apply in a water volume of at least 50 gallons per acre. Transplant the seedlings into the treated band. If planting into a bed, a broadcast application can be made prior to forming the bed. **Foliar sprays for downy mildew:** Make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and downy mildew disease pressure are expected to initiate a disease epidemic. Use the longest interval for preventative applications or very low disease pressure. Shorten the interval as disease pressure and/or fast crop development increases, down to the shortest interval. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 39.5 fl oz per acre per crop growing season. [1 soil application at a maximum of 25.75 fl. oz./A and 5 foliar applications at 2.75 fl. oz./A (13.75 fl. oz./A) per application] The Pre-Harvest Interval (PHI) for these listed crops is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Carrot	Cavity spot, Root Dieback, Forking (*Pythium ultimum*, *P. violae*, *P. sulcatum*, *P. irregular*, *P. splendens*)	6 (0.156)	**Resistance Management:** DO NOT apply more than 5 sprays of Ranman 400SC per crop. Alternate sprays of Ranman 400SC with a fungicide with a different mode of action. **Application Instructions:** Pre-plant incorporated (broadcast or band): Apply in sufficient water to obtain adequate coverage within 3 days of planting and mechanically till into the soil to a depth of at least 2 inches or incorporate with at least 1/4 inch of water. Surface applications (broadcast or band): Subsequent applications may be made beginning at 14 days after plant emergence and continue on a 14-21 day schedule. Apply in sufficient water to obtain adequate coverage with the applications directed to the base of the plant. Ranman 400SC should be incorporated into the soil with ½ to 1 inch of water. If irrigation is not immediately available after the application, then the application should be made in sufficient water to allow penetration into the soil. Ranman 400SC may be applied via any overhead irrigation system. Follow directions outlined in the Application and Calibration Techniques For Sprinkler Irrigation section of the label. Ranman 400SC should be applied during the last 2 hours of the irrigation cycle to allow for adequate soil penetration. For banded applications a 6 to 8 inch band is recommended (See formula to calculate amount required in the band). Calculate the amount of Ranman 400SC needed for band treatments by the formula: $\frac{\text{band width in inches}}{\text{row spacing in inches}} \times \text{broadcast rate per acre} = \text{amount needed per acre of field}$ **Restrictions** DO NOT use more than 30 fl oz per growing season. DO NOT use any adjuvant when applying to carrots. DO NOT apply within 14 days of harvest. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
CUCURBIT VEGETABLE: CROP GROUP 9 Cantaloupe Chayote Chinese-waxgourd Citron Melon Cucumbers Gherkin Gourds Honeydew melons Momordica spp. Muskmelon Watermelon Pumpkin Squash Zucchini	Downy mildew (*Pseudoperonospora cubensis)*	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six sprays of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions:** For Downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning with initial flowering or when disease conditions are favorable for disease development, but prior to disease development. Use the low rate and long interval as disease preventative sprays or when disease conditions are low. Increase to highest rate and shortest interval under moderate to heavy disease pressure. For Phytophthora blight control, apply RANMAN 400SC to the base of the plants at the time of transplanting. Alternatively, RANMAN 400SC may be applied in transplant water at the time of transplanting. Apply 2.75 fl oz per acre in the transplant water. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7- to 10-day schedule beginning when conditions are favorable for disease development. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 50 gallons per acre. RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions following this section. **Restrictions** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop group is 0-day. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Phytophthora blight (*Phytophthora capsici*)	2.75 (0.071)	

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
GRAPES East of the Rocky Mountains	Downy mildew *(Plasmopara viticola)*	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six sprays of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions:** For Downy mildew control, make fungicide applications on a 10- to 14-day schedule beginning when warning systems forecast disease infection periods or when disease conditions are favorable for disease development. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. Do not use any surfactant with this application. Application water volumes for ground applications should be at least 100 gallons per acre. RANMAN 400SC may be applied via aerial application using a minimum of 5 gallons of water volume per acre. **Restrictions** DO NOT apply more than 16.5 fluid ounces (0.43 lb. AI) per acre per growing season. The Pre-Harvest Interval (PHI) for this crop is 30 days.
HOPS	Downy mildew *(Pseudoperonospora humuli)*	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six applications of RANMAN 400SC per crop. Alternate foliar sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions** For downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and downy mildew disease pressure are expected to initiate a disease epidemic. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. Use water spray volume of at least 100 gallons per acre. **Restrictions:** DO NOT apply more than 16.5 fl oz per acre per crop growing season. The Pre-Harvest Interval for this listed crop is 3 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Leafy Greens; Crop Subgroup 4A **Amaranth (leafy amaranth, Chinese spinach, tampala); Arugula (Roquette); Chervil; Edible-leaved chrysanthemum Garland chrysanthemum Corn salad; Garden cress; Upland cress (yellow rocket, winter cress); Dandelion; Dock (sorrel); Endive (escarole); Lettuce (head and leaf); Orach; Parsley; Garden purslane; Winter purslane; Radicchio (red chicory); Spinach; New Zealand spinach; Vine spinach (Malabar spinach, Indian spinach).**	White rust (*Albugo occidentalis*)	2.75 (0.071)	**Resistance Management:** DO NOT apply more than six applications of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions** For white rust control, make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and white rust disease pressure are expected to initiate a disease epidemic. Use the longest interval for preventative applications or very low disease pressure, shortening the interval as disease pressure and/or fast crop development increases up to the shortest interval. For downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning when disease first appears or when disease conditions are favorable for disease development. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase application frequency to the shortest interval under moderate to heavy disease pressure. For Pythium control, make the first application to the soil as a directed, post transplant or post planting application. Make this application within 24 hours of transplanting or seeding. The directed application should be made as a band 4 to 6 inches wide over the seed line or transplants. Direct the entire per-acre rate into the band. Calculate the application rate using the row width. Then, irrigate within 24 hours of the first application with one half (1/2) to one (1) inch of water to properly move the product into the root zone. Alternatively, RANMAN 400SC may be applied in transplant water at the time of transplanting. Do not use a surfactant with this soil drench application. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7- to 10-day schedule beginning when conditions are favorable for disease development. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop group is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Downy mildew (*Bremia lactucae*)	2.75 (0.071)	
	Pythium Damping-off (*Pythium spp.*)	2.75 (0.071)	

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Succulent-podded and Succulent-shelled Beans: ***Cicer arietinum* (chickpea, garbanzo bean);** ***Lupinus* spp. (including sweet lupine, white sweet lupine, white lupine, and grain lupine).** ***Phaseolus* spp. (including kidney bean, lima bean, mung bean, navy bean, pinto bean, snap bean, and waxbean);** ***Vicia faba* (broad bean, fava bean);** ***Vigna* spp. (including asparagus bean, blackeyed pea and cowpea).**	Cottony leak (Pythium aphanidermatum) Pythium ultimum) Downy mildew *(Phytophthora phaseoli)* Phytophthora blight (*Phytophthora capsici*)	2.75 (0.071)	**Resistance Management:** **DO NOT apply more than six applications of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC.** **Application Instructions** **For cottony leak control, make the initial application at full bloom (1st pods) and repeat on a 7- to 14-day schedule. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase application frequency to the shortest interval under moderate to heavy disease pressure.** **For control of downy mildew on lima beans, make the applications on a 7- to 10-day schedule beginning when disease first appears or when disease conditions are favorable for disease development. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase the application frequency to the shortest interval under moderate to heavy disease pressure.** **For Phytophthora blight control, make the 1st application at 100% bloom-pin pod development and a 2nd application at late pin-small pod development and repeat every 7 days as needed to maintain disease control.** **RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 60 gallons per acre.** **RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label.** **Restrictions:** **DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season.** **DO NOT apply to cowpeas used for livestock feed.** **The Pre-Harvest Interval (PHI) for this crop group is 0 days.** **Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.**

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Tuberous and Corm Vegetables: Crop Subgroup 1C **Arracacha; arrowroot; Chinese artichoke; Jerusalem artichoke; Edible canna; Bitter cassava; Sweet Cassava; Chayote (root); Chufa; Dasheen (taro); Ginger; Leren; Potato; Sweet potato; Tanier; Turmeric; Yam bean; True yam**	Late blight *(Phytophthora infestans)* Taro Leaf Blight *(Phytophthora colocasease)*	**Foliar** 1.4 to 2.75 (0.036 to 0.071)	**Resistance Management:** DO NOT apply more than 10 sprays of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. For pink rot Pythium root and crown rot control, do not use **RANMAN 400SC** at reduced rates as incomplete control may occur promoting potential for development of resistant strains. Rotate other fungicides with a different mode of action or tank-mix these fungicides with **RANMAN 400SC** to reduce the chance of resistance occurring. Development of resistance cannot be predicted. If a treatment of **RANMAN 400SC** is not effective, a resistant strain of fungi may be present. Accordingly, neither **RANMAN 400SC** nor other fungicides with a similar mode of action will effectively control the disease. Consult your local State University for alternative recommendations. **Application Instructions:** For foliar blight control, make fungicide applications on a 7- to 10-day schedule beginning when warning systems forecast disease infection periods, generally at row closure or when conditions are favorable for disease development. Use the low rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. For Late blight tuber rot control, make the last 2 to 3 applications prior to desiccation with RANMAN 400SC at 2.75 fl. oz. applied weekly.
	Pink Rot *(Phytophthora erythroseptica)* Pythium Root & Crown Rot *(Pythium spp.)*	**At Planting:** 0.42 fl. oz./ 1000 linear ft [Equivalent to 6.1 fl. oz./A on 36"row spacing] (0.158) **Lay-by/Hilling:** 2.75 fl. oz. /A (0.071)	For pink rot, Pythium root and crown rot control at planting, apply 0.42 fluid ounces of product per 1000 linear foot of row in-furrow at planting using a minimum of 5 gallons of water per acre. Apply RANMAN 400SC using a 6 to 8 inch band directly over the seed pieces prior to furrow closure. A side dressing of RANMAN 400SC applied at hilling may be necessary for additional control. Where mefenoxam-resistant strains of *Phytophthora erythroseptica* and *Pythium* species are not present, a full rate of RANMAN 400SC can be tank-mixed with mefenoxam containing fungicides for additional control. For additional control of Pink Rot, Pythium root and crown rot in combination with an at-planting, in-furrow, RANMAN 400SC application, apply RANMAN 400SC as a broadcast spray at 2.75 fluid ounces in a minimum of 20 gallons of finished spray solution per acre at hilling. Additional applications may be needed depending on susceptibility of the crop to pink, root and/or crown rot disease, environmental conditions conducive to favor severe disease development, or fields located in long growing season areas, etc. Follow the guidelines for disease resistance management listed above. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 50 gallons per acre.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Potato (continued)			RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions following this section. **Restrictions** DO NOT apply more than 27.5 fluid ounces (0.71 lb a.i.) per acre per growning season. DO NOT apply within 7 days of harvest. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
FRUITING VEGETABLES: Crop Group 8-10) includes: African eggplant; BushTomato; Bell pepper; Concona; Currant tomato; Eggplant; Garden huckleberry; Goji berry; Ground Cherry; Martynia; Naranjilla; Okra; Pea eggplant; Pepino; Nonbell pepper; Roselle; Scarlet eggplant; Sunberry; Tomatillo; Tomato; Tree tomato; Cultivars, varieties, and/or hybrids of these.	Late blight (*Phytophthora infestans*)	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six sprays of RANMAN 400SC per crop. Alternate sprays of RANMAN 400SC with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN 400SC followed by at least three applications of fungicides having different modes of action before applying additional RANMAN 400SC. **Application Instructions:** For Late blight control, make fungicide applications on a 7- to 10-day schedule beginning when warning systems forecast disease infection periods, generally at flower initiation or when conditions are favorable for disease development. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval.
	Phytophthora blight (*Phytophthora capsici*)	2.75 (0.071)	For Phytophthora blight control, apply RANMAN 400SC to the base of the plants at the time of transplanting. Alternatively, RANMAN 400SC may be applied in transplant water at the time of transplanting. Apply 2.75 fl oz per acre in the transplant water. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7- to 10-day schedule beginning when conditions are favorable for disease development. RANMAN 400SC should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN 400SC may be applied through sprinkler irrigation equipment. See calibration directions following this section. **Restrictions** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season . The Pre-Harvest Interval (PHI) for these listed crops is 0 day. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Tomato Greenhouse Transplants (Soil Drench)	Pythium Damping-off (*Pythium spp.*)	3 fl oz/100 gallons water (0.078 lb a.i./ 100 gallons water)	**Tomato Greenhouse Transplant Production:** For control of damping-off caused by *Pythium spp.* make a single fungicide application to the seedling tray at the time of planting or at any time thereafter up until 1 week before transplanting. Apply the fungicide solution as a drench to thoroughly wet the growing medium. This results in the use of approximately 1 pint of solution per square foot if the growing medium is 4 inches deep. Do not use any surfactant with this drench application.

APPLICATION AND CALIBRATION TECHNIQUES FOR SPRINKLER IRRIGATION

Apply this product only through center pivot, motorized lateral move, traveling gun, solid set or portable (wheel move, side roll, end tow, or hand move) irrigation system(s). DO NOT apply this product through any other type of irrigation system.

Crop injury, lack of effectiveness, or illegal pesticide residues in the crop can result from non-uniform distribution of treated water.

If you have questions about calibration, you should contact State Extension Service specialists, equipment manufacturers or other experts.

DO NOT apply RANMAN 400SC through irrigation systems connected to a public water system. "Public water system" means a system for the provision to the public of piped water for human consumption if such system has at least 15 service connections or regularly serves an average of at least 25 individuals daily at least 60 days per year.

Controls for both irrigation water and pesticide injection systems must be functionally interlocked, so as to automatically terminate pesticide injection when the irrigation water pump motor stops. A person knowledgeable of the irrigation system and responsible for its operation shall be present so as to discontinue pesticide injection and make necessary adjustments, should the need arise.

The irrigation water pipeline must be fitted with a functional, automatic, quick-closing check valve to prevent the flow of treated irrigation water back toward the water source. The pipeline must also be fitted with a vacuum relief valve and low-pressure drain, located between the irrigation water pump and the check valve, to prevent back-siphoning of treated irrigation water into the water source.

Always inject RANMAN 400SC into irrigation water after it discharges from the irrigation pump and after it passes through the check valve. Never inject pesticides into the intake line on the suction side of the pump.

Pesticide injection equipment must be fitted with a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump. Interlock this valve to the power system, so as to prevent fluid from being withdrawn from the chemical supply tank when the irrigation system is either automatically or manually turned off.

The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump. The irrigation line or water pump must include a functional pressure switch that will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.

Spray mixture in the chemical supply tank must be agitated at all times, otherwise settling and uneven application may occur. DO NOT apply when wind speed favors drift beyond the area intended for treatment.

RANMAN 400SC may be used through two basic types of sprinkler irrigation systems as outlined in Sections A and B below. Determine which type of system is in place, then refer to the appropriate directions provided for each type.

A. Center Pivot, Motorized Lateral Move and Traveling Gun Irrigation Equipment

For injection of pesticides, these continuously moving systems must use a positive displacement injection pump of either diaphragm or piston type, constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock and capable of injection at pressures approximately 2-3 times those encountered within the irrigation water line. Venturi applicator units cannot be used on these systems.

Thoroughly mix recommended amount of this product for acreage to be covered into the same amount of water used during calibration and inject into system continuously for one revolution or run. Mixture in the chemical supply tank must be continuously agitated during the injection run. Shut off injection equipment after one revolution or run, but continue to operate irrigation system until this product has been cleared from the last sprinkler head.

B. Solid Set and Portable (Wheel Move, Side Roll, End Tow, or Hand Move) Irrigation Equipment

With stationary systems, an effectively designed in-line venturi applicator unit is preferred which is constructed of materials that are compatible with pesticides; however, a positive-displacement pump can also be used.

Determine acreage covered by sprinkler. Fill tank of injection equipment with water and adjust flow to use contents over a 30 to 45 minute period. Mix desired amount of RANMAN 400SC for acreage to be covered with water so that the total mixture of this product plus water in the injection tank is equal to the quantity of water used during calibration.

Agitation is recommended. RANMAN 400SC can be injected at the beginning or end of the irrigation cycle or as a separate application. Stop injection equipment after treatment is completed and continue to operate irrigation system until this product has been cleared from last sprinkler head.

WARRANTY AND LIMITATION OF DAMAGES

Seller warrants to those persons lawfully acquiring title to this product that at the time of first sale of this product by Seller that this product conformed to its chemical description and was reasonably fit for the purposes stated on the label when used in accordance with Seller's directions under normal conditions of use. To the extent consistent with applicable law, Buyers and users of this product assume the risk of any use contrary to such directions. **EXCEPT AS PROVIDED ELSEWHERE IN WRITING CONTAINING AN EXPRESS REFERENCE TO THIS WARRANTY AND LIMITATION OF DAMAGES, SELLER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY OR GUARANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR OF MERCHANTABILITY, AND NO AGENT OF SELLER IS AUTHORIZED TO DO SO.** In no event shall Seller's liability for any breach of warranty or guaranty exceed the purchase price of the product as to which a claim is made. To the extent consistent with applicable law, Buyers and users of this product are responsible for all loss or damage from use or handling of this product which results from conditions beyond the control of Seller, including, but not limited to, incompatibility with other products unless otherwise expressly provided in Directions for Use of this product, weather conditions, cultural practices, moisture conditions or other environmental conditions outside of the ranges that are generally recognized as being conducive to good agricultural and/or horticultural practices.

ISK Biosciences Corporation
7470 Auburn Road, Suite A
Concord, Ohio 44077 U.S.A.

Ranman - 120906

Appendix 2

FMC Current Supplemental Label (EPA Reg. No. 71512-3-279)

(This label was the most recent label in the marketplace prior to the newest EPA-approved label (i.e., 10/01/12))

GROUP	21	FUNGICIDE

RANMAN®

FUNGICIDE

EPA Reg. No. 71512-3-279 EPA Est. No. 279-NY-1

Active Ingredient:

Cyazofamid*	34.5%
Other Ingredients:	65.5%
	100.0%

*4-chloro-2-cyano-*N*,*N*-dimethyl-5-(4-methylphenyl)-1*H*-imidazole-1-sulfonamide (CA)

Contains 3.33 pounds Cyazofamid Per Gallon (400 grams per liter)

KEEP OUT OF REACH OF CHILDREN

CAUTION

See other panels for additional precautionary information.

Read entire label carefully and use only as directed.

MANUFACTURED IN FRANCE.

Manufactured for:

FMC

FMC Corporation
Agricultural Products Group
1735 Market Street
Philadelphia PA 19103

Net Contents: 1 Gallon

FIRST AID	
If on skin	• Take off contaminated clothing. • Rinse skin immediately with plenty of soap and water for 15-20 minutes. • Call a poison control center or doctor for treatment advice.
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice
Have the product container or label with you when calling a poison control center or doctor, or going for treatment.	
HOTLINE NUMBER	
For **24-Hour Medical Emergency Assistance** (Human or Animal) Call **1-800-331-3148.** For **Chemical Emergency,** Spill, Leak, Fire or Accident, Call **1-800-331-3148.**	

PRECAUTIONARY STATEMENTS
Hazards to Humans (and Domestic Animals)

CAUTION

Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Avoid breathing spray mist. DO NOT take internally.

Personal Protective Equipment (PPE)

Applicators and other handlers must wear long-sleeved shirt and long pants, socks, shoes, and chemical resistant gloves made of any waterproof material.

Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing. Do not allow contact of contaminated clothing with unprotected skin. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Control Statements
When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240 (d) (4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

IMPORTANT: When reduced PPE is worn because a closed system is being used, handlers must be provided all PPE specified above for "applicators and other handlers" and have such PPE immediately available for use in an emergency, such as a spill or equipment break-down.

User Safety Recommendations

Users Should:

- Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.
- Remove and wash contaminated clothing before reuse.

Environmental Hazards

DO NOT apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. DO NOT contaminate waters when disposing of equipment wash waters or rinsate.

AVOIDING SPRAY DRIFT AT THE APPLICATION SITE IS THE RESPONSIBILITY OF THE APPLICATOR. The interaction of many equipment-and-weather-related factors determine the potential for spray drift. The applicator is responsible for considering all these factors when making decisions. Where states have more stringent regulations, they must be observed.

STORAGE AND DISPOSAL

DO NOT contaminate water, food or feed by storage or disposal. Open dumping is prohibited.

Pesticide Storage: Store in original container, in a secured, dry place separate from fertilizer, food, and feed.

Pesticide Disposal: Pesticide wastes are toxic. Improper disposal of excess pesticide, pesticide spray or rinsate is a violation of Federal law. If these wastes cannot be disposed of by use according to label instructions, contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.

Container Disposal: Nonrefillable container. DO NOT reuse or refill this container. Triple rinse container (or equivalent) promptly after emptying. Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank and drain for 10 seconds after the flow begins to drip. Fill the container 1/4 full with water and recap. Shake for 10 seconds. Pour rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Drain for 10 seconds after the flow begins to drip. Repeat this procedure two more times. Then offer for recycling if available, or puncture and dispose of in a sanitary landfill, or by incineration or, if allowed by state and local authorities, by burning. If burned, stay out of smoke.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

FAILURE TO FOLLOW THE USE DIRECTIONS AND PRECAUTIONS ON THIS LABEL MAY RESULT IN PLANT INJURY OR POOR DISEASE CONTROL.

Do not use for disease control on fruiting vegetables (other than tomato transplants) or cucurbit vegetables grown for fruit production in greenhouses.

ROTATIONAL CROP RESTRICTIONS

Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

DO NOT apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURE USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR Part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted-entry interval. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

DO NOT enter or allow worker entry into treated areas during the restricted entry interval (REI) of twelve (12) hours.

PPE required for early entry to the treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: coveralls, chemical resistant gloves made of any waterproof material, shoes plus socks and protective eyewear.

GENERAL INFORMATION

MIXING AND SPRAYING

RANMAN FUNGICIDE can be used effectively in dilute or concentrate sprays. Thorough, uniform coverage is essential for disease control.

NOTE: Slowly invert container several times to assure uniform mixture of formulation before adding this product to the spray tank.

Dosage rates on this label indicate fluid ounces of RANMAN FUNGICIDE per acre, unless otherwise stated. Under conditions favorable for disease development, the highest rate specified and shortest application interval should be used. For best product performance in all applications utilizing water volumes up to 60 gallons per acre, an organosilicone surfactant should be added according to the manufacturer's label recommendations in order to improve spray coverage when the disease infection is severe. However, a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant may be used according to the manufacturer's label when disease infection is moderate or light. Do not use a surfactant in applications to grapes or tomato greenhouse transplant production.

RANMAN FUNGICIDE may be applied with all types of spray equipment normally used for ground and aerial applications.

The required amount of RANMAN FUNGICIDE should be added slowly into the spray tank during filling. With concentrate sprays, premix the required amount of RANMAN FUNGICIDE in a clean container and add to the spray tank as it is being filled. Keep agitator running when filling spray tank and during spray operations. DO NOT allow spray mixture to stand overnight or for prolonged periods. Prepare only the amount of spray required for immediate use. Spraying equipment should be thoroughly cleaned immediately after the application.

Apply RANMAN FUNGICIDE in sufficient water to obtain adequate coverage of the foliage. Gallonage to be used will vary with crop and amount of plant growth. Spray volume will usually range from 20 to 100 gallons per acre (200 to 1000 liters per hectare) for dilute sprays, and 5 to 10 gallons per acre (50 to 100 liters per hectare) for concentrate ground and aerial sprays. For aerial applications, apply RANMAN FUNGICIDE in a minimum of 5 gallons of water per acre. Application through sprinkler irrigation systems is not recommended unless specific directions are given for a crop. See application and calibration instruction below.

TANK MIX COMPATIBILITY

RANMAN FUNGICIDE is physically compatible (no nozzle or screen blockage) with many products recommended for control of diseases and insects on vegetable crops. Read and follow all manufacturer's label recommendations for the tank mix companion product. It is the applicator's responsibility to ensure that the companion product is EPA approved for use on the intended crop. RANMAN FUNGICIDE is generally compatible with other insecticides, fungicides, fertilizers and micronutrient products provided sufficient free water is available for dispersion of all the tank mix products. However, the physical compatibility of RANMAN FUNGICIDE with tank mix partners must be evaluated before use. Conduct a jar test with intended tank-mix pesticides prior to preparation of large volumes. Use the following procedure: 1) Pour the recommended proportions of the products into a suitable container of water, 2) Mix thoroughly and 3) Allow to stand 5 minutes. If the combination remains mixed or can be re-mixed readily, it is considered physically compatible. Any physical incompatibility in the jar test indicates that RANMAN FUNGICIDE should not be used in the tank-mix.

RANMAN FUNGICIDE is physically compatible (no nozzle or screen blockage) with the following list of products:

Product	Active Ingredient
Acrobat	dimethomorph
Chlorothalonil (several)	chlorothalonil
Curzate	cymoxanil
EDBC (several)	mancozeb
Headline /Cabrio	pyraclostrobin
Mineral oils	
Omega	fluazinam
Previcur	Propamocarb hydrochloride
Quadris /Abound	azoxystrobin

CROP RESPONSE

RANMAN FUNGICIDE is not phytotoxic to the crop or succeeding crops when applied according to label instructions.

INTEGRATED PEST MANAGEMENT

RANMAN FUNGICIDE is an excellent disease control agent when used according to label directions for control of several Oomycete fungi. Although RANMAN FUNGICIDE has limited systemic activity, it should be utilized as a protectant fungicide and applied before the disease infects the crop. Depending upon the level of disease pressure, good protection of the crop against disease can be expected over a period of 7 to 10 days. RANMAN FUNGICIDE is recommended for use as part of an Integrated Pest Management (IPM) program, which may include the use of disease-resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting and disease forecasting systems aimed at preventing economic pest damage. Practices known to reduce disease development should be followed. Consult your state cooperative extension service or local agricultural authorities for additional IPM strategies established in your area. RANMAN FUNGICIDE may be used in State Agricultural Extension advisory (disease forecasting) programs that recommend application timing based upon environmental factors that favor disease development.

RESISTANCE MANAGEMENT

Some plant pathogens are known to develop resistance to products used repeatedly for disease control. RANMAN FUNGICIDE's mode/target site of action is complex III of fungal respiration: ubiquinone reductase, Qi site, FRAC code 21. A disease management program that includes alternation or tank mixes between RANMAN FUNGICIDE and other labeled fungicides that have a different mode of action and/or control pathogens not controlled by RANMAN FUNGICIDE is essential to prevent disease resistant pathogens populations from developing. RANMAN FUNGICIDE should not be utilized continuously nor tank mixed with fungicides that have shown to have developed fungal resistance to the target disease.

Since pathogens differ in their potential to develop resistance to fungicides, follow the directions outlined in the "Directions For Use" section of this label for specific resistance management strategies for each crop. Consult with your Federal or State Cooperative Extension Service representatives for guidance on the proper use of RANMAN FUNGICIDE in programs that seek to minimize the occurrence of disease resistance. RANMAN FUNGICIDE is not cross-resistant with other classes of fungicides that have different modes of action.

DIRECTIONS FOR USE

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Basil	**Downy mildew** *(Peronospora belbahrii)*	2.75 to 3.0 (0.071 to 0.078)	**Resistance Management:** DO NOT apply more than 9 applications of RANMAN Fungicide per crop. Alternate sprays of RANMAN Fungicide with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN Fungicide followed by at least three applications of fungicides having different modes of action before applying additional RANMAN Fungicide. **Application Instructions:** For control of downy mildew on basil, make the applications on a 7- to 10-day schedule beginning when disease conditions are favorable for disease development. Use the lower rate and longest interval as disease preventative sprays or when disease conditions are low. Increase to the highest rate and shortest interval under moderate to heavy disease pressure. RANMAN Fungicide can be applied on basil grown in a greenhouse. RANMAN Fungicide should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 50 to 75 gallons per acre. RANMAN Fungicide may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 27 fluid ounces (0.7 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
BRASSICA (COLE) LEAFY VEGETABLES: CROP GROUP 5 Broccoli; Chinese broccoli (gai lon); broccoli raab (rapini); Brussels sprouts; cabbage; Chinese cabbage (bok choy); Chinese cabbage (napa); Chinese mustard (gai choy); cauliflower; cavalo broccolo; collards; kale; kohlrabi; mizuna; mustard greens; mustard spinach; rape greens; turnip greens	**Club root** *(Plasmodiophora brassicae)* **Downy mildew** *(Peronospora parasitica)*	**Transplant Soil Drench:** 12.9 to 25.75 (0.333 to 0.665 per 100 gallons **Soil Incorporation:** 20 / A (0.52) **Foliar:** 2.75 / A (0.072)	**Resistance Management:** DO NOT apply more than six (1 soil + 5 foliar) applications of RANMAN Fungicide per crop. Alternate foliar sprays of RANMAN Fungicide with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN Fungicide followed by at least three applications of fungicides having different modes of action before applying additional RANMAN Fungicide. **Application Instructions:** **Transplant Soil Drench for control of club root:** Immediately after transplanting, make a single application within the rate range listed and apply 1.7 fluid ounces of solution per plant as transplant water. Use the lowest rate for fields with low soil infestation and increase to the higher rates when fields have a history of moderate to high soil infestation. **Soil Incorporation:** Alternatively, if desired and for soil with low infiltration rates, apply 20 fl oz per acre in a minimum bandwidth of 9 inches along the planting row and incorporate to a soil depth of 6 to 8 inches with a precision incorporator in the same operation. Apply in a water volume of at least 50 gallons per acre. Transplant the seedlings into the treated band. If planting into a bed, a broadcast application can be made prior to forming the bed. **Foliar sprays for downy mildew:** Make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and downy mildew disease pressure are expected to initiate a disease epidemic. Use the longest interval for preventative applications or very low disease pressure. Shorten the interval as disease pressure and/or fast crop development increases, down to the shortest interval. RANMAN Fungicide should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN Fungicide may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 39.5 fl oz per acre per crop growing season. [1 soil application at a maximum of 25.75 fl. oz./A and 5 foliar applications at 2.75 fl. oz./A (13.75 fl. oz./A) per application] The Pre-Harvest Interval (PHI) for these listed crops is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz Product Per Acre (lb. ai/A)	Instructions
Carrot	Cavity spot, Root Dieback, Forking *(Pythium ultimum, P. violae, P. sulcatum, P. irregulare, P. splendens)*	6 (0.156)	**Resistance Management:** DO NOT apply more than 5 sprays of Ranman per crop. Alternate sprays of Ranman with a fungicide with a different mode of action. **Application instructions:** Pre-plant incorporated (broadcast or band): Apply in sufficient water to obtain adequate coverage within 3 days of planting and mechanically till into the soil to a depth of at least 2 inches or incorporate with at least 1/4 inch of water. Surface applications (broadcast or band): Subsequent applications may be made beginning at 14 days after plant emergence and continue on a 14-21 day schedule. Apply in sufficient water to obtain adequate coverage with the applications directed to the base of the plant. Ranman should be incorporated into the soil with ½ to 1 inch of water. If irrigation is not immediately available after the application, then the application should be made in sufficient water to allow penetration into the soil. Ranman may be applied via any overhead irrigation system. Follow directions outlined in the Application and Calibration Techniques For Sprinkler Irrigation section of the label. Ranman Fungicide should be applied during the last 2 hours of the irrigation cycle to allow for adequate soil penetration. For banded applications a 6 to 8 inch band is recommended (See formula to calculate amount required in the band). Calculate the amount of Ranman needed for band treatments by the formula: $\frac{\text{band width in inches}}{\text{row spacing in inches}} \times \text{broadcast rate per acre} = \text{amount needed per acre of field}$ **Restrictions:** DO NOT use more than 30 fl oz per growing season. DO NOT use any adjuvant when applying to carrots. DO NOT apply within 14 days of harvest. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
CUCURBIT VEGETABLE CROP GROUP 9 Cantaloupe Chayote Chinese waxgourd Citron Melon Cucumbers Gherkin Gourds Honeydew melons Momordica spp. Muskmelon Watermelon Pumpkin Squash Zucchini	Downy mildew (*Pseudoperonospora cubensis*) Phytophthora blight (*Phytophthora capsici*)	2.1 to 2.75 (0.054 to 0.071) 2.75 (0.071)	**Resistance Management:** DO NOT apply more than six sprays of RANMAN FUNGICIDE per crop. Alternate sprays of RANMAN FUNGICIDE with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN FUNGICIDE followed by at least three applications of fungicides having different modes of action before applying additional RANMAN FUNGICIDE. **Application instructions:** For Downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning with initial flowering or when disease conditions are favorable for disease development, but prior to disease development. Use the low rate and long interval as disease preventative sprays or when disease conditions are low. Increase to highest rate and shortest interval under moderate to heavy disease pressure. For Phytophthora blight control, apply RANMAN FUNGICIDE to the base of the plants at the time of transplanting. Alternatively, RANMAN FUNGICIDE may be applied in transplant water at the time of transplanting. Apply 2.75 fl oz per acre in the transplant water. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7 to 10 day schedule beginning when conditions are favorable for disease development. RANMAN FUNGICIDE should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 50 gallons per acre. RANMAN FUNGICIDE may be applied through sprinkler irrigation equipment. See calibration directions preceding this section. **Restrictions:** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop group is 0-day. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
GRAPES East of the Rocky Mountains	Downy mildew (*Plasmopara viticola*)	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six sprays of RANMAN FUNGICIDE per crop. Alternate sprays of RANMAN FUNGICIDE with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN FUNGICIDE followed by at least three applications of fungicides having different modes of action before applying additional RANMAN FUNGICIDE. **Application instructions:** For Downy mildew control, make fungicide applications on a 10- to 14-day schedule beginning when warning systems forecast disease infection periods or when disease conditions are favorable for disease development. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. Do not use any surfactant with this application. Application water volumes for ground applications should be at least 100 gallons per acre. RANMAN FUNGICIDE may be applied via aerial application using a minimum of 5 gallons of water volume per acre. **Restrictions** DO NOT apply more than 16.5 fluid ounces (0.43 lb. AI) per acre per growing season. The Pre-Harvest Interval (PHI) for this crop is 30 days.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
HOPS	**Downy mildew** (*Pseudoperonospora humuli*)	2.1 to 2.75 (0.054 to 0.071)	**Resistance Management:** DO NOT apply more than six applications of RANMAN Fungicide per crop. Alternate foliar sprays of RANMAN Fungicide with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN Fungicide followed by at least three applications of fungicides having different modes of action before applying additional RANMAN Fungicide. **Application Instructions** For downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and downy mildew disease pressure are expected to initiate a disease epidemic. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. Use water spray volume of at least 100 gallons per acre. **Restrictions:** DO NOT apply more than 16.5 fl oz per acre per crop growing season. The Pre-Harvest Interval for this listed crop is 3 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Leafy Greens; Crop Subgroup 4A Amaranth (leafy amaranth, Chinese spinach, tampala); Arugula (Roquette); Chervil; Edible-leaved chrysanthemum Garland chrysanthemu mCorn salad; Garden cress; Upland cress (yellow rocket, winter cress); Dandelion; Dock (sorrel); Endive (escarole); Lettuce (head and leaf); Orach; Parsley; Garden purslane; Winter purslane; Radicchio (red chicory); Spinach; New Zealand spinach; Vine spinach (Malabar spinach, Indian spinach).	**White rust** *(Albugo occidentalis)*	2.75 0.071)	**Resistance Management:** DO NOT apply more than six applications of RANMAN Fungicide per crop. Alternate sprays of RANMAN Fungicide with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN Fungicide followed by at least three applications of fungicides having different modes of action before applying additional RANMAN Fungicide. **Application Instructions** For white rust control, make fungicide applications on a 7- to 10-day schedule beginning when disease is first seen or weather and white rust disease pressure are expected to initiate a disease epidemic. Use the longest interval for preventative applications or very low disease pressure, shortening the interval as disease pressure and/or fast crop development increases up to the shortest interval. For downy mildew control, make fungicide applications on a 7- to 10-day schedule beginning when disease first appears or when disease conditions are favorable for disease development. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase application frequency to the shortest interval under moderate to heavy disease pressure. For Pythium control, make the first application to the soil as a directed, post transplant or post planting application. Make this application within 24 hours of transplanting or seeding. The directed application should be made as a band 4 to 6 inches wide over the seed line or transplants. Direct the entire per-acre rate into the band. Calculate the application rate using the row width. Then, irrigate within 24 hours of the first application with one half (1/2) to one (1) inch of water to properly move the product into the root zone. Alternatively, RANMAN Fungicide may be applied in transplant water at the time of transplanting. Do not use a surfactant with this soil drench application. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7- to 10-day schedule beginning when conditions are favorable for disease development. RANMAN Fungicide should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN Fungicide may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for this crop group is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Downy mildew *(Bremia lactucae)*	2.75 (0.071)	
	Pythium Damping-off *(Pythium spp.)*	2.75 (0.071)	

Crop	Diseases	Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Succulent-podded and Succulent-shelled Beans: *Cicer arietinum* (chickpea, garbanzo bean); *Lupinus* spp. (including sweet lupine, white sweet lupine, white lupine, and grain lupine). *Phaseolus* spp. (including kidney bean, lima bean, mung bean, navy bean, pinto bean, snap bean, and waxbean); *Vicia faba* (broad bean, fava bean); *Vigna* spp. (including asparagus bean, black-eyed pea and cowpea).	**Cottony leak** *(Pythium aphanidermatum)* *Pythium ultimum)*	2.75 (0.071)	**Resistance Management:** DO NOT apply more than six applications of RANMAN Fungicide per crop. Alternate sprays of RANMAN Fungicide with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN Fungicide followed by at least three applications of fungicides having different modes of action before applying additional RANMAN Fungicide . **Application Instructions** For cottony leak control, make the initial application at full bloom (1st pods) and repeat on a 7- to 14-day schedule. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase application frequency to the shortest interval under moderate to heavy disease pressure. For control of downy mildew on lima beans, make the applications on a 7- to 10-day schedule beginning when disease first appears or when disease conditions are favorable for disease development. Use the longest interval for disease preventative sprays or when disease conditions are low. Increase the application frequency to the shortest interval under moderate to heavy disease pressure. For Phytophthora blight control, make the 1st application at 100% bloom-pin pod development and a 2nd application at late pin-small pod development and repeat every 7 days as needed to maintain disease control. RANMAN Fungicide should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendation for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 60 gallons per acre. RANMAN Fungicide may be applied through sprinkler irrigation equipment. See calibration directions elsewhere on the label. **Restrictions:** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. DO NOT apply to cowpeas used for livestock feed. The Pre-Harvest Interval (PHI) for this crop group is 0 days. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Downy mildew *(Phytophthora phaseoli)*		
	Phytophthora blight *(Phytophthora capsici)*		

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
Tuberous and Corm Vegetables: Crop Subgroup 1C Arracacha; arrowroot; Chinese artichoke; Jerusalem artichoke; Edible canna; Bitter cassava; Sweet Cassava; Chayote (root); Chufa; Dasheen (taro); Ginger; Leren; Potato; Sweet potato; Tanier; Turmeric; Yam bean; True yam	Late blight (*Phytophthora infestans*) Taro Leaf Blight *(Phytophthora colocasease)*	**Foliar** 1.4 to 2.75 (0.036 to 0.071)	**Resistance Management:** DO NOT apply more than 10 sprays of RANMAN FUNGICIDE per crop. Alternate sprays of RANMAN FUNGICIDE with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN FUNGICIDE followed by at least three applications of fungicides having different modes of action before applying additional RANMAN FUNGICIDE. For pink rot, Pythium root and crown rot control, do not use RANMAN FUNGICIDE at reduced rates as incomplete control may occur promoting potential for development of resistant strains. Rotate other fungicides with a different mode of action or tank-mix these fungicides with RANMAN FUNGICIDE to reduce the chance of resistance occurring. Development of resistance cannot be predicted. If a treatment of RANMAN FUNGICIDE is not effective, a resistant strain of fungi may be present. Accordingly, neither RANMAN FUNGICIDE nor other fungicides with a similar mode of action will effectively control the disease. Consult your local State University for alternative recommendations. **Application instructions:** For foliar blight control, make fungicide applications on a 7- to 10-day schedule beginning when warning systems forecast disease infection periods, generally at row closure or when conditions are favorable for disease development. Use the low rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. For Late blight tuber rot control, make the last 2 to 3 applications prior to desiccation with RANMAN FUNGICIDE at 2.75 fl. oz. applied weekly. For pink rot, Pythium root and crown rot control at planting, apply 0.42 fluid ounces of product per 1000 linear foot of row in-furrow at planting using a minimum of 5 gallons of water per acre. Apply RANMAN FUNGICIDE using a 6 to 8 inch band directly over the seed pieces prior to furrow closure. A side dressing of RANMAN FUNGICIDE applied at hilling may be necessary for additional control. Where mefenoxam-resistant strains of *Phytophthora erythroseptica* and *Pythium species* are not present, a full rate of RANMAN FUNGICIDE can be tank-mixed with mefenoxam containing fungicides for additional control. For additional control of Pink Rot, Pythium root and crown rot in combination with an at-planting, in-furrow, RANMAN FUNGICIDE application, apply RANMAN FUNGICIDE as a broadcast spray at 2.75 fluid ounces in a minimum of 20 gallons of finished spray solution per acre at hilling. Additional applications may be needed depending on susceptibility of the crop to pink, root and/or crown rot disease, environmental conditions conducive to favor severe disease development, or fields located in long growing season areas, etc. Follow the guidelines for disease resistance management listed above. RANMAN FUNGICIDE should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 20 to 50 gallons per acre. RANMAN FUNGICIDE may be applied through sprinkler irrigation equipment. See calibration directions preceding this section. **Restrictions** DO NOT apply more than 27.5 fluid ounces (0.71 lb a.i.) per acre per year growning season. DO NOT apply within 7 days of harvest. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Pink Rot *(Phytophthora erythroseptica)* Pythium Root & Crown Rot *(Pythium spp.)*	**At Planting:** 0.42 fl. oz./ 1000 linear ft [Equivalent to 6.1 fl. oz./A on 36"row spacing] (0.158) **Lay-by/Hilling:** 2.75 fl. oz. /A (0.071)	

Crop	Diseases	Use Rate Fl. Oz. Product Per Acre (lb. ai/A)	Instructions
FRUITING VEGETABLES (Crop Group 8-10) and OKRA, includes: African eggplant; Bush Tomato; Bell pepper; Concona; Currant tomato; Eggplant; Garden huckleberry; Goji berry; Ground Cherry; Martynia; Naranjilla; Okra; Pea eggplant; Pepino; Nonbell pepper; Roselle; Scarlet eggplant; Sunberry; Tomatillo; Tomato; Tree tomato; Cultivars, varieties, and/or hybrids of these.	Late blight (*Phytophthora infestans*)	2.1 to 2.75 (0.054 to 0.0710	**Resistance Management:** DO NOT apply more than six sprays of RANMAN FUNGICIDE per crop. Alternate sprays of RANMAN FUNGICIDE with a fungicide with a different mode of action. DO NOT make more than three consecutive applications of RANMAN FUNGICIDE followed by at least three applications of fungicides having different modes of action before applying additional RANMAN FUNGICIDE. **Application instructions:** For Late blight control, make fungicide applications on a 7- to 10-day schedule beginning when warning systems forecast disease infection periods, generally at flower initiation or when conditions are favorable for disease development. Use the lowest rate and longest interval for preventative applications or very low disease pressure, increasing the rate and shortening the interval as disease pressure and/or fast crop development increases up to the maximum rate and shortest interval. For Phytophthora blight control, apply RANMAN FUNGICIDE to the base of the plants at the time of transplanting. Alternatively, RANMAN FUNGICIDE may be applied in transplant water at the time of transplanting. Apply 2.75 fl oz per acre in the transplant water. It is recommended that the water volume for this initial application be at least 50 gallons per acre. Additional applications should be made on a 7 to 10 day schedule beginning when conditions are favorable for disease development. RANMAN FUNGICIDE should be tank-mixed with an organosilicone surfactant when the disease infection is severe, or a non-ionic surfactant or a blend of an organosilicone and a non-ionic surfactant when disease infection is moderate or light, at the manufacturer's label recommendations for water volumes up to 60 gallons per acre. Normal water volumes are 30 to 60 gallons per acre. RANMAN FUNGICIDE may be applied through sprinkler irrigation equipment. See calibration directions preceding this section. **Restrictions** DO NOT apply more than 16.5 fluid ounces (0.43 lb a.i.) per acre per crop growing season. The Pre-Harvest Interval (PHI) for these listed crops is 0-day. Crops on this label may be planted immediately after the last treatment. Do not plant other crops not registered for this product within 30 days after the last application.
	Phytophthora blight *(Phytophthora capsici)*	2.75 (0.071)	
Tomato Greenhouse Transplants (Soil Drench)	Pythium Damping-off (*Pythium spp.*)	3 fl oz/100 gallons water (0.078 lb a.i./ 100 gallons water)	**Tomato Greenhouse Transplant Production:** For control of damping-off caused by Pythium spp. make a single fungicide application to the seedling tray at the time of planting or at any time thereafter up until 1 week before transplanting. Apply the fungicide solution as a drench to thoroughly wet the growing medium. This results in the use of approximately 1 pint of solution per square foot if the growing medium is 4 inches deep. Do not use any surfactant with this drench application.

APPLICATION AND CALIBRATION TECHNIQUES FOR SPRINKLER IRRIGATION

Apply this product only through center pivot, motorized lateral move, traveling gun, solid set or portable (wheel move, side roll, end tow, or hand move) irrigation system(s). DO NOT apply this product through any other type of irrigation system.

Crop injury, lack of effectiveness, or illegal pesticide residues in the crop can result from non-uniform distribution of treated water.

If you have questions about calibration, you should contact State Extension Service specialists, equipment manufacturers or other experts.

DO NOT apply RANMAN FUNGICIDE through irrigation systems connected to a public water system. "Public water system" means a system for the provision to the public of piped water for human consumption if such system has at least 15 service connections or regularly serves an average of at least 25 individuals daily at least 60 days per year.

Controls for both irrigation water and pesticide injection systems must be functionally interlocked, so as to automatically terminate pesticide injection when the irrigation water pump motor stops. A person knowledgeable of the irrigation system and responsible for its operation shall be present so as to discontinue pesticide injection and make necessary adjustments, should the need arise.

The irrigation water pipeline must be fitted with a functional, automatic, quick-closing check valve to prevent the flow of treated irrigation water back toward the water source. The pipeline must also be fitted with a vacuum relief valve and low-pressure drain, located between the irrigation water pump and the check valve, to prevent backsiphoning of treated irrigation water into the water source.

Always inject RANMAN FUNGICIDE into irrigation water after it discharges from the irrigation pump and after it passes through the check valve. Never inject pesticides into the intake line on the suction side of the pump.

Pesticide injection equipment must be fitted with a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump. Interlock this valve to the power system, so as to prevent fluid from being withdrawn from the chemical supply tank when the irrigation system is either automatically or manually turned off.

The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump. The irrigation line or water pump must include a functional pressure switch that will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.

Spray mixture in the chemical supply tank must be agitated at all times, otherwise settling and uneven application may occur. DO NOT apply when wind speed favors drift beyond the area intended for treatment.

RANMAN FUNGICIDE may be used through two basic types of sprinkler irrigation systems as outlined in Sections A and B below. Determine which type of system is in place, then refer to the appropriate directions provided for each type.

A. Center Pivot, Motorized Lateral Move and Traveling Gun Irrigation Equipment

For injection of pesticides, these continuously moving systems must use a positive displacement injection pump of either diaphragm or piston type, constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock and capable of injection at pressures approximately 2-3 times those encountered within the irrigation water line. Venturi applicator units cannot be used on these systems.

Thoroughly mix recommended amount of this product for acreage to be covered into the same amount of water used during calibration and inject into system continuously for one revolution or run. Mixture in the chemical supply tank must be continuously agitated during the injection run. Shut off injection equipment after one revolution or run, but continue to operate irrigation system until this product has been cleared from the last sprinkler head.

B. Solid Set and Portable (Wheel Move, Side Roll, End Tow, or Hand Move) Irrigation Equipment

With stationary systems, an effectively designed in-line venturi applicator unit is preferred which is constructed of materials that are compatible with pesticides; however, a positive-displacement pump can also be used.

Determine acreage covered by sprinkler. Fill tank of injection equipment with water and adjust flow to use contents over a 30 to 45 minute period. Mix desired amount of RANMAN FUNGICIDE for acreage to be covered with water so that the total mixture of this product plus water in the injection tank is equal to the quantity of water used during calibration.

Agitation is recommended. RANMAN FUNGICIDE can be injected at the beginning or end of the irrigation cycle or as a separate application. Stop injection equipment after treatment is completed and continue to operate irrigation system until this product has been cleared from last sprinkler head

WARRANTY AND LIMITATION OF DAMAGES

Seller warrants to those persons lawfully acquiring title to this product that at the time of first sale of this product by Seller that this product conformed to its chemical description and was reasonably fit for the purposes stated on the label when used in accordance with Seller's directions under normal conditions of use. To the extent consistent with applicable law, Buyers and users of this product assume the risk of any use contrary to such directions.

EXCEPT AS PROVIDED ELSEWHERE IN WRITING CONTAINING AN EXPRESS REFERENCE TO THIS WARRANTY AND LIMITATION OF DAMAGES, SELLER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY OR GUARANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR OF MERCHANTABILITY, AND NO AGENT OF SELLER IS AUTHORIZED TO DO SO.

In no event shall Seller's liability for any breach of warranty or guaranty exceed the purchase price of the product as to which a claim is made. To the extent consistent with applicable law, Buyers and users of this product are responsible for all loss or damage from use or handling of this product which results from conditions beyond the control of Seller, including, but not limited to, incompatibility with other products unless otherwise expressly provided in Directions for Use of this product, weather conditions, cultural practices, moisture conditions or other environmental conditions outside of the ranges that are generally recognized as being conducive to good agricultural and/or horticultural practices.

Appendix 3

USDA NASS Information for Cyazofamid Labeled Crops

APPENDIX 3: USDA NASS INFORMATION FOR CYAZOFAMID LABELED CROPS

Commodity	Acreage*	Minor Use Eligibility
Crop Group 5		
Broccoli	130,603	Yes
Broccoli, Chinese	N/A	Yes
Broccoli, raab	N/A	Yes
Brussels sprouts	3,874	Yes
Chinese cabbage, (bok choy)	11,480	Yes
Chinese cabbage, (napa)		Yes
Chinese mustard cabbage	66	Yes
Cabbage	80,620	Yes
Cauliflower	39,515	Yes
Cavalo broccoli	N/A	Yes
Collards	11,223	Yes
Kale	3,994	Yes
Kohlrabi	N/A	Yes
Mizuna	N/A	Yes
Mustard greens	8,323	Yes
Mustard spinach	N/A	Yes
Rape greens	1,600	Yes
Turnip greens	9,365	Yes
Crop Group 8		
Tomato	442,225	No
Eggplant	6.038	Yes
Ground cherry	n/a	Yes
Okra	2,444	Yes
Pepino	n/a	Yes
Bell pepper	Bell pepper excluding pimentos: 62,363	Yes
Chili pepper	Peppers other than bell: 37,372	Yes
Cooking pepper	Peppers other than bell: 37,372	Yes
Pimento	Peppers other than bell: 37,372	Yes
Sweet pepper	Peppers other than bell: 37,372	Yes
Tomatillo	N/A	Yes

APPENDIX 3: USDA NASS INFORMATION FOR CYAZOFAMID LABELED CROPS - CONTINUED

Commodity	Acreage*	Minor Use Eligibility
Crop Group 9		
Cantaloupe	84,290	Yes
Crop Group 9		
Chayote	n/a	Yes
Chinese waxgourd (Chinese preserving melon)	n/a	Yes
Citron-melon	n/a	Yes
Cucumber	Cucumber/pickles: 151,759	Yes
Gherkin	n/a	Yes
Gourd	n/a	Yes
Honeydew melon	17,344	Yes
Momordica spp.	n/a	Yes
Muskmelon	n/a	Yes
Watermelon	142,359	No
Pumpkin	92,955	Yes
Squash	54,454	Yes
Zucchini	n/a	Yes
Carrot	90.292	Yes
Potato	1,131,963	No
Grape, East of the Rocky Mountains	102,829= 1,051,407 (US total) – 868,330 (California) – 61,056 (Washington) – 18,192 (Oregon)	Yes
Tomato, Greenhouse Transplant	43,949,871 sqft = 1,009 acres	Yes
Spinach	44,071	Yes
Hop	31,145	Yes

*USDA NASS Database. Unless otherwise noted, data retrieved from the 2007 Agricultural Census.
N/A= Not Available, but assumed below the 300,000 acre threshold and thus considered minor crops.