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Evaluating Fungicide Recommendations for Vegetable Crops in the United States: Should More Be Done to Limit the Risk of Fungicide Resistance Development?

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Abstract: Fungicides are an important component of Integrated Pest Management (IPM) programs developed for vegetable produc Without fungicides, commercial vegetable production would not be economically feasible in many regions of the U.S. Recommendations for fungicide use in commercial vegetable production are developed and delivered by Extension in state and reg production guides. Efforts have been made by the chemical industry and Extension to increase the awareness of fungicide resistanc development. The article reviews fungicide resistance development and management and current progress and areas of needed improvement in fungicide resistance management guidelines developed for commercial vegetable production in the U.S.

Introduction

In 2001, $31.8 billion (USD) were spent on pesticides world-wide (Keily, Donaldson, & Grube, 2004). In the U.S. alone, fungicide comprised 8% ($835 million) of all pesticide expenditures, with $615 million spent on fungicides for agricultural use (Keily, Donaldson, & Grube, 2004). Agricultural fungicides are necessary to control important diseases in many different crops and cropp systems (Keily, Donaldson, & Grube, 2004). In 2005, it was estimated that an economic return of $14.60 was achieved for each do spent on fungicide in the U.S. (Gianessi & Riegner, 2005). Without the use of fungicides or other pesticides (i.e., herbicides or insecticides), many vegetable crops could not be economically grown in many parts of the U.S. and other parts of the world.

Development of Fungicide Resistance Risks and Use of FRAC Codes

In the early 1980s, an industry-lead group known as the Fungicide Resistance Action Committee, or FRAC, was established to hel identify existing and potential fungicide resistance management issues and provide guidelines (FRAC, 2009). Since that time, FRA committees have been established throughout Europe, North and South America, and Japan to manage and monitor fungicide resis development. Each year the FRAC committee publishes a list of FRAC codes that contains most of the fungicides and fungicide chemistries where modes-of-action and resistance-risks are known.

To date, there are 43 numbered and three lettered FRAC codes for the approximately 86 chemical codes and 171 common names o fungicides listed (FRAC, 2009). Accordingly, fungicides listed within a given FRAC code may share a similar mode-of-action and therefore have similar risks for resistance development and similar use patterns on single or multiple crops, and they may also exhi the potential for cross-resistance development. Other industry-sponsored resistance management groups have been established to monitor resistance development in weeds (Herbicide Resistance Action Committee, HRAC) and insect pests (Insecticide Resistanc Action Committee, IRAC).

Importance of Risk Management

Because certain pesticide chemistries have more specific modes of action, there is a much greater chance for some pests (e.g., plan pathogens, as well as weeds and insect pests) to develop resistance to them. For example, fungi that produce a vast number of asex conidia or undergo multiple disease cycles during a given production season (e.g., *Podosphaera xanthii* causing cucurbit powdery mildew) (McGrath, 2001), or fungi that have a high probability for sexual reproduction in field populations (e.g., *P. infestans* causi late blight of potato and tomato) (Lee, Mizubuti, & Fry, 1999) often have a much greater chance for fungicide resistance developm Importantly, in cases where only a few, high-resistance risk fungicides are available for disease control, selection pressure put on t pathogen may be intensified by the repeated application of the same or similar fungicide chemistries.

The grouping of similar fungicides together by resistance group code (i.e., FRAC code) and the inclusion of resistance managemen guidelines on fungicide labels were designed to reduce the chances for resistance development and help agricultural producers dev and follow resistance management programs. Although application restrictions and resistance management guidelines have been developed by the chemical industry, the adoption of such guidelines has been left solely to the individual applicator. Jutsum, Hean Perrin, and Wege (1998) pointed out that the challenge was to develop resistance management strategies that are relevant to local production practices.

In recent years, the use of FRAC, HRAC, and IRAC codes has been widely included in state and regional commercial vegetable production recommendations and are promoted and used by Extension personnel and crop advisors as education and teaching tools many vegetable production regions of the U.S. However, even with increased awareness, the proper use of these pesticides is ultim placed upon the end-user applicator to make sure that the pesticides are properly applied according to the label rate, its restrictions state and federal laws.

Fungicide Resistance Development

Benzimidazole Fungicides

The first reported case of resistance development in vegetable production in the U.S. was during 1969 to 1970, when cucurbit pow mildew fungi developed resistance to the benzimidazole fungicide, benomyl (FRAC, or Fungicide Resistance Action Committee, c 1) (McGrath, 2001; Morton & Staub, 2008). Benzimidazoles have a single-site mode of action and work by inhibiting microtubule assembly during mitosis (Morton & Staub, 2008). These compounds were subject to misuse, largely due to their low use rate, broa spectrum of activity, and ability to protect new growth (e.g., xylem-mobile) (Morton & Staub, 2008). Benomyl was voluntarily removed from the market and is no longer recommended in vegetable production because of resistance issues; however, other benzimidazole chemistries within the same FRAC group, such as thiothanate-methyl, are still recommended for control of some important soil-borne fungal pathogens (FRAC, 2009). The development of resistance to benzimidazole fungicides is known to exis at least 100 plant pathogens (Genet, 2005).

Triazole Fungicides

During the 1970s and 1980s, dozens of triazole fungicides (FRAC code 3) were developed and released with successive chemistrie offering some advantages over their earlier predecessors (Russell, 2005). Triazole fungicides (e.g., imidazoles, piperazines, pyrimidines, triazoles), also known as demethylation inhibitors (DMIs), affect fungal growth and development by inhibiting ergost production, which is a key component in the cell wall structure of some types of fungi. Fungicide resistance development to DMIs developed shortly after their introduction in some cropping systems (Russell, 2005). Action taken by FRAC and the fungicide manufacturers in developing resistance management strategies (e.g, such as restricting the number of applications per season) has helped to make the triazoles one of the largest and most successful classes of fungicide chemistries to date (Russell, 2005). Triazol fungicides are used on a limited basis in vegetable production, mostly for the control of cucurbit powdery mildew (*Podosphaera xanthii*) where fungicide resistance is already known to exist to them (McGrath, 2001; Wyenandt, Maxwell, & Ward, 2008).

Strobilurin (QoI) Fungicides

In the late 1990s, strobilurin fungicides, which were originally derived from the basidiomycete *Strobilurus tenacellus* and produce naturally occurring fungicidal compound known as -methoxy-acrylic acid, were released for use in U.S. vegetable production (McGrath, 2001). Strobilurin fungicides have protectant, systemic and eradicant activities, although different compounds from the group have different properties (Russell, 2005; Bartlett, Clough, Godwin, Hall, Hamer, & Par-Dobrzanski, 2002). All strobilurin, o QoI fungicides (FRAC code 11), share the same biological mode-of-action by binding at the Qo site on cytochrome b inhibiting mitochondrial respiration (Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008; FRAC, 2009; McGrath, 2001). The first strobilurin fungicides were available for use in 1996 and they quickly became one of the most important groups of agricultural fungicides. Unfortunately, resistance was reported in Europe within 2 years of their introduction (Deising, Reimann, & Pascholati, 2008; Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008; Russell, 2005).

A number of single-site nucleotide polymorphisms confer resistance to QoI fungicides in a number of different fungal species. To the most common polymorphism is the single amino acid substitution of a guanine to adenine at site 143 in QoI-resistant isolates. T is commonly referred to as "G143A resistance" and is known to be qualitative in nature. Other single site substitutions include F12 and G137R, where resistant isolates express moderate (or partial) resistance, and control in the field is usually maintained at recommended fungicide rates (Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008). Importantly, G143A resistance has b detected in more than 20 species of fungi and fungal-like organisms, including many ascomycetes (powdery mildews) and oomyce (downy mildews), as well as in some species of *Alternaria* (Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008). Once QoI-resistance develops within a given fungal population, the selection pressure placed on the population eventually leads to resist in the entire population, and any other use of strobilurin chemistry (i.e., other FRAC code 11 fungicides) is completely ineffective (McGrath, 2001; Wyenandt, Maxwell, & Ward, 2008).

Strobilurin fungicides accounted for over 20% of the global fungicide market within the first 10 years of their commercial release (Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008). Azoxystrobin (FRAC code 11) is one of the world's most common applied fungicides (Bartlett, Clough, Godwin, Hall, Hamer, & Par-Dobrzanski, 2002; Fernandez-Ortuno, Tores, De Vicente, & Perez-Garcia, 2008), and is used extensively in vegetable production to control a wide range of important fungal pathogens.

Phenylamide Fungicides

Other groups of fungicides, such as the phenylamides (FRAC code 4), which include mefenoxam and metalaxyl, are widely used i vegetable production to control root and crown rots caused species of *Pythium* and *Phytothphora*. Resistance and/or insensitivity to both of these chemistries are widespread in the U.S. in important pathogens of vegetable crops such as *Phytophthora infestans, P. erythroseptica* and *P. capsici* (Lamour & Hausbeck, 2000, 2003; Lee, Mizubuti, & Fry, 1999; Parra & Ristaino, 2001; Taylor, Pas & Gudmestad, 2006).

Newest Groups of Fungicides

In recent years, a number of fungicides with new modes-of-action have been released for use in vegetable production. These incluc quinolines (quinoxyfen, FRAC code 13), which affect signaling in fungal cells; carboxamides (boscalid, FRAC code 7), which aff fungal respiration; aniline-pyrimidines (cyprodinil, FRAC code 9), which affect methionine biosynthesis in fungal cells; and cyanomidazoles (cyazofamid, FRAC code 21), which affect complex III (Qi site) in fungal respiration. Importantly, all of the aforementioned fungicides have medium or high risks for resistance development and require resistance management (FRAC, 200 list of commonly used fungicides, along with their active ingredients and FRAC codes, in commercial vegetable production in the is presented in Table 1.

Table 1.
List of Fungicides, Active Ingredients, and FRAC Codes for Some Commonly Used Fungicides in Commercial Vegetable Produc in the United States

Fungicide(s)	Active Ingredient(s)	FRAC Code
Copper	fixed copper(s)	M1
Sulfur	sulfur	M2
Mancozeb, Maneb, Dithane	EBDC	M3
Captan	captan	M4
Chlorothalonil	chlorothalonil	M5
Topsin M	thiophanate-methyl	1
Nova, Procure, Tilt	myclobutanil, triflumizole, propiconizole	3
Ridomil Gold Copper	mefenoxam + copper	4 + M1
Ridomil Gold Bravo	mefenoxam + chlorothalonil	4 + M5
Ridomil Gold, Ultra Flourish	mefenoxam	4
Endura	boscalid	7
Switch	cyprodinil + fludioxonil	9 + 12
Quadris	azoxystrobin	11
Cabrio	pyraclostrobin	11
Flint	trifloxystrobin	11
Pristine	pyraclostrobin + boscalid	11 + 7
Reason	fenamidone	11
Tanos	fomoxadone + cymoxanil	11 + 27
Elevate	fenhexamid	17
Ranman	cyazofamid	21
Gavel	zoxamide + mancozeb	22 + M3
Curzate	cymoxanil	27
Previcur Flex	propomocarb HCL	28
Alliete, Phosphonates	fosetyl Al, phosphorous acids	33
Forum	dimethomorph	40

Vegetable Disease Control Recommendations in the United States

A current search determined that 47 states offer fungicide recommendations for vegetable disease control in a hardcopy or on-line format (Table 2). Of those, five regional (multi-state) recommendation guides representing 28 states (in total) are developed on an annual or bi-annual basis (Table 2). Regional vegetable production guides with disease control recommendations include the mid-Atlantic region (NJ, PA, DE, MD, VA and WV), Northeast region (ME, NH, VT, MA, CT and RI), High Plains region (CO, N MT and WY), Southeast region (NC, SC, GA, LA, MS and AL), and Mid-West region (IN, IL, IA, KS and MO) of the U.S. Ten o states including KY, MI, FL, TX, TN, CA, WI, OH, NY, NM, and AR develop their own vegetable recommendation guidelines (T 2). The two states with the most vegetable production acreage in the United States, FL and CA, each produce their own vegetable disease control recommendations.

Table 2.

State and/or Region, Host of Publication, Type of Publication, Publish Period, Publish Format, and FRAC codes and Resistanc Management Guidelines Included in Commercial Vegetable Disease Control Recommendations in the Continental United States Alaska and Hawaii

State/Region	Host of Publication	Type of Publication	Publish Period	Publish Format	FRAC Codes	Resistance Guidelines
New England	collaborative extension website	recommendation guide	bi-annually	H/O	Y	Y
Mid Atlantic	cooperative extension	recommendation guide	annually	H/O	Y	Y
Southeast	cooperative extension	recommendation guide	annually	H/O	Y	Y
Midwest	cooperative extension	recommendation guide	annually	H/O	Y	Y
High Plains	collaborative extension website	recommendation guide	updated	H/O	N	N
Kentucky	university print services	recommendation guide	bi-annually	H/O	Y	Y
Michigan	cooperative extension	recommendation guide	updated	H/O	N	Y
Florida	cooperative extension	recommendation guide	annually	H/O	Y	Y
Texas	cooperative extension	recommendation guide	annually	H/O	N	N
California	cooperative extension	recommendation guide	annually	H/O	Y	Y
Wisconsin			annually	H/O	Y	Y

	cooperative extension	recommendation guide				
Ohio	cooperative extension	recommendation guide	annually	H/O	Y	Y
New York	cooperative extension	recommendation guide	annually	H/O	Y	Y
New Mexico	NPIRS	online, label search only	updated	H/O	N	N
Tennessee	cooperative extension	recommendation guide	annually	H/O	N	Y
Arizona	none	none	none	(-)	(-)	(-)
Nevada	none	none	none	(-)	(-)	(-)
Utah	cooperative extension	fact sheets	updated	H/O	N	N
North Dakota	cooperative extension	fact sheets	updated	H/O	N	N
South Dakota	cooperative extension	none, link to other site	none	(-)	N	N
Arkansas	cooperative extension	recommendation guide	annually	H/O	N	Y
Oklahoma	cooperative extension	recommendation guide	annually	H/O	Y	Y
Alaska	cooperative extension	crop profiles only	updated	H/O	N	N

Internet website addresses for information related to commercial vegetable fungicide recommendation guidelines by state or regior collected for this review are presented in Table 3. Vegetable disease control recommendations are available in hardcopy on an ann basis for some states (e.g., OH, MI, and FL) and regions (i.e., Mid-Atlantic region) or in alternate years (i.e., KY or the Northeast region). State or regional vegetable disease control recommendations may include a "laundry list" of fungicides currently registere use or include only those chemistries with the highest efficacy for disease control. For example, because each state or region devel its own recommendations independent of other states or regions, a fungicide recommended in one state or region may not be recommended in a nearby state or region.

Table 3.

Internet Website Addresses for States and/or Regions That Produce Vegetable Disease Control Recommendations in the United S

State/Region	Internet Address
New England	http://www.nevegetable.org
Mid Atlantic	http://www.njveg.rutgers.edu

Southeast	http://www.lsuagcenter.com/en/crops_livestock/crops/vegetables/
Midwest	http://www.ag.purdue.edu/btny/Extension/Pages/extpubs.aspx
High Plains	http://wiki.bugwood.org/Main_Page
Kentucky	http://www.ca.uky.edu/agc/pubs/id/id36/id36.htm
Michigan	http://web2.msue.msu.edu/bulletins/subjectsearch.cfm
Florida	http://edis.ifas.ufl.edu/document_pg100
Texas	http://aggie-horticulture.tamu.edu/extension/vegetable/cropguides/
California	http://www.ipm.ucdavis.edu/PMG/crops-agriculture.html
Wisconsin	http://learningstore.uwex.edu/Commercial-Vegetable-Production-in-Wisconsin2009-P540C103.aspx
Ohio	http://ohioline.osu.edu/b672/
New York	http://www.nysaes.cornell.edu/recommends/
New Mexico	http://state.ceris.purdue.edu/htbin/stweb.com
Tennessee	http://www.utextension.utk.edu/publications/pests/default.asp#commercial
Arizona	none
Nevada	none
Utah	http://utahpests.usu.edu/plantdiseases/htm/vegetable
North Dakota	http://www.ag.ndsu.edu/pubs/plntdise.html
South Dakota	http://sdces.sdstate.edu/ces_website/horticulture_bottom.cfm?category=Vegetables&news=Vegetables&subject=Veg
Arkansas	http://www.uaex.edu/Other_Areas/publications/HTML/MP-154.asp
Oklahoma	http://entoplp.okstate.edu/factshts.htm
Alaska	http://www.alaskapestmanagement.com/pesticide_lables.htm
Hawaii	http://www.ctahr.hawaii.edu/ctahr2001/PIO/FreePubs.asp
Oregon	http://ipmnet.org/plant-disease/intro.cfm
Utah	none
Washington	http://wsprs.wsu.edu/

Table 3 includes Internet website addresses for state and/or regional vegetable production recommendations. In some cases, for regio recommendations, only one website from a state in that region is listed (i.e. Mid-Atlantic, Southeast).

In theory, if one were to look for a recommendation for a federally labeled fungicide one could go to one of 17 different resources information based on the total number of regional and/or states offering commercial vegetable disease control recommendations in United States. Although a federally labeled fungicide is legally allowed to be applied according to the label in any given state acco to state guidelines, the use of that fungicide may or may not be recommended. Applicators should always check with their local extension service or crop consultant before applying any fungicides.

Implications of Fungicide Recommendations by States or Regions

Because individual states and/or regions generate their own recommendations, the potential to develop broad-scale geographic fungicide resistance management recommendations may be severely limited. For example, cucurbit powdery mildew is an extreme important pathogen in vegetable production. The two pathogen's that cause cucurbit powdery mildew, *Podosphaera xanthii* or *Golovinomyces cucurbitacearum*, are obligate parasites that originate in southern Florida and disseminate up the East Coast in the spring and summer via weather patterns. Because high-risk fungicides, such as the strobilurins (FRAC code 11), are recommended control of powdery mildew in the Southeast region, there is a high probability for a strobilurin-resistant powdery mildew populatio enter in the Mid-Atlantic and Northeast region each summer. Therefore, the likelihood of successfully controlling the incoming powdery mildew population with strobilurin fungicides becomes severely limited or reduced for much of the mid-Atlantic and Northeast regions. This has occurred in the Mid-Atlantic region, where strobilurin fungicides are no longer recommended for controlling cucurbit powdery mildew because resistance has been detected for a number of growing seasons, (McGrath, 2001; Wyenandt, Maxwell, & Ward, 2008);, but the same strobilurin fungicides remain listed as recommendations for cucurbit powdery mildew control in New York state and the Northeast region.

Efforts in Fungicide Resistance Management in Vegetable Production the United States

The implementation of FRAC codes on fungicide labels by the chemical industry and the addition of FRAC codes in recommendat guidelines are designed to help agricultural producers (e.g., vegetable growers in this instance) develop effective season-long disea control programs while reducing the chances for fungicide resistance development. In many cases, resistance management guidelin are included in state or regional recommendation guides (Table 2). Table 2 includes the list of regions and/or states which offer vegetable disease control recommendations, the developer/distributor of the recommendation guidelines, the type of publication (I hardcopy format and O = available online), the timing of the publication, and whether FRAC codes and/or resistance management guidelines are included in each state or regional guideline.

Recently, fungicide resistance management guidelines for vegetable crops have been developed as supplemental information to reg commercial vegetable production guides or as fungicide resistance management tables for specific diseases on certain crops (Wyer Rideout, Everts, Mulrooney, & Maxwell, 2009; Wyenandt, McGrath, Rideout, Gugino, Everts, & Mulrooney, 2009).

Breakdown on the Use of FRAC Codes and Fungicide Resistance Management Guidelines in Vegetable Disease Control Recommendatio in the U.S.

Currently, there are 17 different sources of fungicide recommendation guidelines (not including fact sheets or crop profiles) for vegetable disease control in the United States (Tables 2 and 3). Of these, only 11 (65%) include the use of FRAC codes and resista management guidelines (Table 2), 14 (82%) include the use of resistance management guidelines for vegetable disease control (Ta 2), 5 (29%) do not include FRAC codes at all, and 3 (18%) do not include the use of fungicide resistance management guidelines. is extremely important, because, although the fungicide label is the law, most commercial vegetable growers use state or regional recommendation guides for determining fungicide use and fungicide rotations for disease control. Additionally, for those states or regions that offer vegetable fungicide recommendations on-line, only a few are available free of charge.

Two states (NM and SD) offer only searchable on-line fungicide label databases, and one state (AZ) makes this type of informatio available at grower/producer meetings. Although useful, on-line databases contain a large number of fungicide labels, and potentia options can be very difficult to sift through and use efficiently. For one state, a link was provided that took the user to another state vegetable disease website, but not directly to the fungicide recommendations. Additionally, for the state that only offered this information at meetings, growers in that state might find it extremely difficult to find out and/or have enough information to make important resistance management decisions, especially if that information in not readily available in a hardcopy format or available on-line.

In many cases, great effort is required to find these on-line resources at state Extension and/or regional websites. For some states, t only information related to commercial vegetable disease control could be found in extension fact sheets or crop profiles that, in so cases, were out of date. This is important because information available on the Internet in outdated fact sheets, crop profiles or on-l recommendation guides may include fungicides that are no longer recommended, no longer legal to apply, and/or no longer effecti This puts the individual using information from these outdated on-line "recommendations" in a precarious situation with potential l consequences.

Conclusions

For fungicide resistance management to become more successful and sustainable, increased cooperation and collaboration, as well more dedicated internal and external funding are needed by state Extension services to properly address fungicide resistance management issues in commercial vegetable production in the U.S. Importantly, educational opportunities on fungicides resistance development must be continually developed and offered to commercial vegetable producers. A simple review of vegetable disease control recommendations for vegetable crops grown in the continental U.S. and Alaska and Hawaii determined that among the 50 states, there are 17 state and/or regional resources for commercial vegetable disease control recommendations. Most of these resou are developed independently of one another, and fungicide recommendations may vary significantly from state to state and/or regio region.

To date, other than the development and use of FRAC codes by the chemical industry, there are no set national standards for the us FRAC codes and/or resistance management guidelines in state or regional commercial vegetable recommendation guides. In most cases, FRAC codes and resistance management sections are included in some format in state and regional recommendation guides. FRAC codes are often included in alphabetized fungicide lists in tables or in different sections of the recommendations guide and n next to the actual recommendation. Although this format may help with the listing and finding of different fungicides by alphabetiz letter, it does nothing to coordinate or group fungicides with similar modes of action (i.e., FRAC codes) together in recommendatio guides. In most cases, the restrictions for uses and/or rotations are included in other parts of the same table or in another section of recommendations guide, which could very easily lead to confusion by the applicator.

More cooperation between those regions that produce their own guidelines (e.g., Southeast and Mid-Atlantic) is strongly needed fo developing long-term, economically and environmentally sustainable fungicide resistance management guidelines for important vegetable diseases such as cucurbit downy and powdery mildew. States or regions that produce their own guidelines need to extend additional help to those states that do not produce guidelines. Although vegetable production may not be an important economic component of the agricultural community in those states, vegetable growers should not be forced to make important decisions with pertinent information. Better use of the Internet for distribution of vegetable disease control recommendations is needed for some s and regions. This is especially important for any vegetable grower seeking information on disease control through their local Exten service.

Information on fungicide use for vegetable disease control needs to be updated yearly, or at least bi-annually, or removed from the Internet once it is deemed out-of-date (i.e., usually in 1 or 2 years) or on-line resources will continue to become an ever increasing "graveyard" of poorly managed, outdated information for vegetable growers. Most importantl, information on fungicide resistance management in vegetable disease control must be readily available, up-to-date, and easily accessible. Implementing a national form standard(s) for using FRAC codes in commercial vegetable production recommendation guidelines must be considered.

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