WATERMELON, CUCUMBER, SQUASH
Meets Criteria III and IV – Resistance management and IPM.
Target pest: Anthracnose of cucurbits, *Colletotrichum orbiculare*.

BELL PEPPER, NON-BELL PEPPER
Meets Criteria III and IV – Resistance management and IPM
Target pest: Anthracnose of pepper, *Colletotrichum gloeosporioides* and *Colletotrichum acutatum*

Executive Summary:

1) Cucurbit anthracnose, caused by *Colletotrichum orbiculare*, is an aggressive and highly destructive disease of cucumber, watermelon and squash that is responsible for significant loss of yield and quality resulting in severe crop losses (https://www.vegetables.cornell.edu/pest-management/disease-factsheets/anthracnose-of-cucurbits/). The disease has become more severe and widespread in recent years, leading to an increased demand in effective tools to control the disease. Climate change is likely to increase the duration of conducive environmental conditions for this disease, which includes warm temperatures and high humidity, and become more severe in the future.
2) Pepper anthracnose, caused primarily by *Colletotrichum gloeosporioides* and *Colletotrichum acutatum* (and occasionally other species), has become an emerging threat in recent years traditionally infecting mostly ripened bell and chili peppers (ripened, red peppers). As with anthracnose disease on cucurbits, pepper anthracnose thrives in warm, moist climates often associated with pepper-growing areas in Florida and in the SE United States. (https://content.ces.ncsu.edu/anthracnose-of-pepper). The last 10 years has seen an increased occurrence of pepper anthracnose, more recently even on green, unripe fruit causing significant yield losses.
3) Benzovindiflupyr (ISO name for Solatenol® Technology, a fungicide contained in Aprovia and Aprovia Top), is an SDHI carboxamide fungicide that is highly active on cucurbit anthracnose, caused primarily by the pathogen *Colletotrichum orbiculare*. Despite other SDHI fungicides now in the market, research has demonstrated that **among the SDHI fungicides labeled on cucurbits, only benzovindiflupyr has sufficient intrinsic activity on the cucurbit anthracnose pathogen to provide commercially acceptable levels of control** (*Ishii H, Zhen F, Hu M, Li X, Schnabel G.: Efficacy of SDHI fungicides, including benzovindiflupyr, against Colletotrichum species. Pest Manag Sci. 2016 Oct;72(10):1844-53. doi: 10.1002/ps.4216. Epub 2016 Feb 9. PMID: 26732510*, https://pubmed.ncbi.nlm.nih.gov/26732510/). Furthermore, benzovindiflupyr has been recognized in the literature as among the most active (or sole active) fungicide to control most species of Colletotrichum, including the species responsible for the disease on pepper (https://pubmed.ncbi.nlm.nih.gov/35249649/). As a result, **benzovindiflupyr is unique within the SDHI's for its ability to provide an efficacious alternate mode of action to current solutions (strobilurin QoI, triazole DMI and multisite fungicides such as chlorothalonil and mancozeb) allowing it to be positioned as an optimal mixture or rotational partner for control of anthracnose**, while maximizing the resistance management and sustainability of chemical control solutions used to manage this important disease. Other SDHI fungicides labeled for control of this disease are combined in mixture with other active fungicides from the DMI or QoI mode of action, and have been shown to have little or no viable intrinsic activity on their own

against *Colletotrichum spp*., instead, depending on the partner active ingredient contained in the fungicide premixture product for control. **As a result, only one carboxamide SDHI labeled for control of anthracnose, benzovindiflupyr (Solatenol ® Technology) is providing commercially viable efficacy against *Colletotrichum spp*., whether solo or in mixture with other fungicides.**

4) Integrated pest management (IPM) practice is identified as deploying various cultural and agronomic practices to ensure management of fungal diseases, and this includes the efficient use of fungicides. However, for fungicides to be considered an optimal tool in an IPM program, the fungicides must be 1) labeled on the crop in question, **2) sufficiently active on the pathogen to provide intrinsic activity** and provide commercially acceptable efficacy, 3) representing a different mode of action that serves to spread the selection pressure against key pathogens across different modes of action and thereby minimizing resistance risk and ensuring longer-term sustainable use. This last point does require that other fungicides within the same mode of action are either not labeled, or not active, on the target pest. Furthermore, the biokinetic properties of the fungicide, for example its ability to adhere longer to the leaf surface or within the wax layer could also contribute to a successful IPM program by extending the duration of control which could reduce the number of overall applications in a given season. **Benzovindiflupyr is the only carboxamide SDHI fungicide labeled for control of anthracnose on cucumber, watermelon, squash and peppers (bell and non-bell) that is sufficiently active enough to qualify as an effective tool that would ensure commercially acceptable levels of efficacy**, and provide selection pressure from a novel mode of action **that would minimize resistance risk** to partner and rotational fungicides in the QoI, DMI and other non-SDHI modes of action targeted to control cucurbit anthracnose. Furthermore, **benzovindiflupyr would be best positioned in an IPM program as providing the best control in combinations with tolerant or resistant varieties, crop rotation, or other practices that would minimize disease pressure and allow optimal preventative disease control**, thereby increasing the effectiveness of a preventative fungicide like benzovindiflupyr. **Other SDHI's introduced into the market have been shown to not be sufficiently intrinsically active on Colletotrichum spp., and therefore most dependent on the partner active ingredient contained in the product formulation**. As a result, although likely active on other pathogens on these crops, the SDHI component is non-contributory (or only weakly active) on anthracnose, and indirectly increasing the risk of resistance and decreasing the value of fungicide contribution to an IPM program.

Therefore, since benzovindiflupyr is described and recognized as the only carboxamide SDHI fungicide active on the pathogen Colletotrichum spp., which is the causal agent of anthracnose disease of cucumbers, watermelon, squash and peppers (bell and non-bell), that this active ingredient represents a novel mode of action for highly efficacious control of this disease and provides both a robust fungicide resistance management tool as well as an appropriate chemical control contribution in a successful IPM program, that this should qualify benzovindiflupyr as a candidate for extended exclusive use under criteria III and IV of FIFRA section 3(c) (1) (F) (ii).

Introduction and Rationale –

Cucurbit anthracnose of cucumber, watermelon and squash:
Cucurbit crops (includes cucumber, watermelon and squash) are affected by an increasingly important disease known as anthracnose, caused by the fungal pathogen *Colletotrichum orbiculare*. Often other species of Colletotrichum can be implicated in anthracnose disease, such as *C. acutatum* and *C. gloeosporioides*; but in cucurbits, *C. orbiculare* is most recognized as the pathogen species implicated in cucurbit anthracnose. Cucurbit anthracnose has become increasingly common in these crops and has proven difficult to control without good integrated pest management (IPM) practices. More information on anthracnose of cucurbits can be found from the 'Vegetable MD online' resource from Cornell University: (http://vegetablemdonline.ppath.cornell.edu/factsheets/Cucurbit_Anthracnose.htm)

Pepper anthracnose of bell pepper and non-bell pepper:
Peppers (including bell and non-bell peppers) are also infected by anthracnose, and the severity and importance of this disease has increased in recent years. Unlike in cucurbits, where one species of Colletotrichum has been implicated as the sole causal agent of anthracnose disease, in peppers the species complex is composed of many species. Most of the recent work on pepper anthracnose has focused on two key species, *C. gloeosporioides* and *C. acuatum*. The former is implicated mostly in ripened, red fruit whereas *C. actuatum* has been reported as having the ability to infect and cause lesions on unripe, green fruit, making *C. acutatum* a much greater threat to pepper production including the more commonly found green bell or chili peppers such as jalapenos (https://www.sciencedirect.com/science/article/pii/S0261219408000963).

Anthracnose disease is highly aggressive and extremely destructive to cucumber, watermelon, squash and peppers (bell and non-bell peppers) especially during warm and moist seasons in the southern, mid-Atlantic, and mid-western states. Warm and moist conditions, considered highly conducive conditions for the presence and spread of this disease, can be expected to be more prevalent in future seasons due to climate change. The disease has increased in economic importance in recent years (Anthracnose of Cucurbits | Cornell Vegetables and Anthracnose on Pepper | Vegetable Pathology – Long Island Horticultural Research & Extension Center (cornell.edu)) Currently, a combination of cultural and chemical control is used to combat and manage this disease, including such IPM practices as 1) ensuring disease-free seed, 2) quality crop rotation with non-host crops in a two-to-three year rotation, 3) sanitation practices to remove or destroy crop residue that could harbor pest inoculum, 4) the use of anthracnose-resistant varieties, and 5) the use of effective fungicide chemistries in combination with 1 – 4 above. No one single use of these practices can be successfully utilized to completely control this highly aggressive disease under conducive environmental conditions, therefore, a combination of these practices (IPM approach) is required to successfully combat this disease and maintain yields that ensure marketability of unblemished and high-quality fruit production. The use of effective chemistry is extremely important to any successful IPM program.

According to University of Minnesota extension, chemistry commonly used to control this disease includes the following for watermelon (https://mwveguide.org/results/pest/379/crops/588), cucumber (https://mwveguide.org/results/pest/379/crops/585), squash (https://mwveguide.org/results/pest/379/crops/587), and pepper (https://mwveguide.org/results/pest/380/crops/582): azoxystrobin, pyraclostrobin, trifloxystrobin, famoxadone (FRAC 11), thiophanate-methyl (FRAC 01), chlorothalonil (FRAC M05), mancozeb (FRAC M03), cyprodinil (FRAC 09), zoxamide (FRAC 22), difenoconazole (FRAC 03), and fluopyram, fluxapyroxad, boscalid, and benzovindiflupyr (FRAC 07). Some of these fungicides occur in product mixtures labeled for anthracnose that contain fungicides not active on ascomycete fungi like *Colletotrichum spp*., such as cymoxanil (FRAC 27) or oxathiapiprolin (FRAC 49), which are active only on oomycetes but offered in mixture with famoxadone or chlorothalonil, respectively, and which will not be addressed here despite the fact they are labeled for control of the disease because they are used in premix with an active partner. Some fungicides in the FRAC group 7, such as penthiopyrad, are labeled for cucurbits but do not contain a label for anthracnose / Colletotrichum spp. on these crops, presumably because they are not sufficiently active on Colletotrichum. On peppers, only suppression is claimed (**see Figure 1**).

The carboxamide SDHI fungicides are a relatively new class of fungicides that have become more widespread in agriculture over the last ten to fifteen years. The most recent introductions fall within the pyrazole-4-carboxamide class of carboxamide chemistry, and have shown improved efficacy overall compared to older carboxamide fungicides, such as boscalid, or the even older actives such as flutolanil or carboxin fungicides. The latter having a much narrower spectrum of activity, limited mostly to a few pathogens in the basidiomycete class of fungi (rusts, Rhizoctonia sp., etc.), and not utilized for control of the more common and economically important ascomycete leaf spot diseases. The timeline of SDHI fungicide introductions spans over several decades (**see Figure 2**), but the introduction of the newer 'pyrazole carboxamides' are the ones most in widespread use today. The SDHI fungicides are respiration-inhibitor fungicides, as are the strobilurin QoI fungicides, but active on a different enzyme within the mitochondrial respiration pathway (complex II versus complex III). This means they often show similar spectrum to the strobilurin fungicides but can offer resistance management potential due to the fact they are not cross-resistant (www.frac.info).

Within the carboxamide SDHI class of fungicides, differences in pathogen spectrum and dose rates can be quite extreme. SDHI fungicides work by binding to the SDH enzyme (complex II) in the mitochondrial respiration pathway located in the mitochondrial membrane within the pathogen cell. The intrinsic activity, or site selectivity, of SDHI's can vary in their ability to bind to the target enzyme which can determine the effective dose needed for sufficient disease control. Benzovindiflupyr has among the highest intrinsic activity among the more common SDHI's which allows for lower rates of active ingredient across both ascomycetes and basidiomycete fungi, as demonstrated for *Septoria tritici* and *Rhizoctonia solani*, respectively (**Figure 3**). The reason for this can be explained by the highly lipophilic nature of the active ingredient, highly attracted to 'oily' (or waxy) hydrophobic environments, such as that exists within the bipolar mitochondrial membrane where the target SDH enzyme is located. In addition, this same characteristic allows a strong adherence to the wax layer of the cucurbit or pepper leaf where the active can stay active and stable for longer periods of time, ensuring some degree of persistence that allows a longer period of disease protection from fungicides containing benzovindiflupyr. In leaf partitioning studies, benzovindiflupyr accumulates and persists in the wax layer to a much greater degree than other SDHI fungicides (**Figure 4**). This characteristic of benzovindiflupyr ensures that fungicides containing this active ingredient are well suited to be part of a robust IPM program that includes the use of disease tolerant crops, planting of disease-free seed, and potentially lowering the number of applications needed to achieve optimal levels of disease control. The longerlasting performance and optimal leaf and fruit protection ensure that crops that started with good IPM program of minimizing seed-borne infection and crop rotation will keep those clean plants even cleaner for longer, and essentially achieving more value from a fungicide application. As such, we believe that benzovindiflupyr remains a key tool within any IPM program for anthracnose management of cucurbit and pepper crops.

The introduction of the SDHI fungicides over the last decade have considerably increased the management tools for growers to manage fungal diseases of cucurbit crops and are complementary to previous fungicide chemistries, such as triazoles and strobilurins, that are prevalent in the market today. While the newer class of SDHI fungicides are represented mostly by the pyrazole-4-carboxamides (**Figure 5**), often simply referred to as pyrazole carboxamides, this class is known to be much more intrinsically active than the older classes of chemistry and tend to represent the most common fungicides used commercially within the Group 7 fungicides. Benzovindiflupyr is among the newer and more modern pyrazole carboxamide class of SDHI fungicides (**Figure 5**), which has been proven to have a much higher intrinsic activity on the pathogen target enzyme than many of the older carboxamide SDHI fungicides due, in part, to its unique molecular structure and lipophilic properties (**Figure 3**).

While these fungicides can provide good resistance management and enhanced efficacy to strobilurin and triazole chemistry, due to offering higher potency with a new mode of action and no cross-resistance, the pathogen spectrum is very important to ensure a robust IPM fit as it pertains to chemical control. While the SDHI fungicides do indeed have the same mode of action, the pathogen spectrum for diseases they control can vary quite significantly! Considering anthracnose disease on cucurbits, caused by *C. orbiculare*, it is very important to understand that most of the fungicides in the SDHI class of chemistry are not found to be active on *Colletotrichum spp*.; and yet while many are labeled to control the disease (often with a partner that is active, such as a triazole and / or strobilurin fungicide), the SDHI component itself is ***not*** necessarily active on *C. orbiculare*, and therefore <u>do not</u> offer a SDHI-based solution for controlling this disease. Research has been conducted to compare the efficacy of benzovindiflupyr to other labeled SDHI fungicides and found that for many economically important species of Colletotrichum spp., including *C. orbiculare, C. acutatum and C. gloeosporioides* that **only benzovindiflupyr provided the required intrinsic activity on the pathogen** that would lead to commercially acceptable levels of control of anthracnose **(Figure 6).** From this research it is clear than of all the labeled SDHI fungicides on cucumber, watermelon, squash or pepper to control anthracnose disease, do not provide sufficient efficacy of the disease and instead, relay solely on the partner active ingredient contained in the premixture fungicide product (ie. the triazole or strobilurin component). Unfortunately, for those products that contain a strobilurin as the active partner labeled for control of *Colletotrichum spp*., QoI resistance is widespread and therefore such products may not provide acceptable efficacy on this disease in cucurbits or peppers. In fact, it would be disadvantageous to assume a product containing an SDHI and QoI would be a reliable product to manage this disease in light of the excessive reports of QoI resistance (www.frac.info), and the fact that most SDHI fungicides have little or no efficacy against *Colletotrichum spp*. (**Figure 7**), which includes *C. orbiculare* on cucurbits as well as *C. gloeosporioides* and *C. acutatum*, the main anthracnose pathogens on bell pepper and non-bell peppers. As such, products containing benzovindiflupyr, such as Aprovia or Aprovia Top, ensure a more robust product concept for management of this disease as these products contain either an active

SDHI fungicide (benzovindiflupyr) or in mixture with a triazole DMI fungicide (difenoconazole), and not the QoI chemistry which has many documented cases of resistance to *Colletotrichum spp*.

As stated by Robert Guenther with United Fresh Produce Association during the registration comment period for benzovindiflupyr (EPA-HQ-OPP-2013-0141-0041), the importance of this new chemistry as providing (among other points not listed here): 1) broad spectrum fungicide in the FRAC group 7, and 2) incorporates a greater diversity of active ingredients in rotation, which helps maintain the utility of other active ingredients. Subsequent knowledge that **benzovindiflupyr is among the only group 7 fungicide registered with proven efficacy on *C. orbiculare, C. gloeosporioides, and C. acutatum*** makes this statement even more relevant despite having other SDHI alternatives available in the market. Indeed, out of all other SDHIs labeled on these crops the remaining group 7's in the market are either not labeled for anthracnose or labeled for suppression only (penthiopyrad on cucurbits and peppers, respectively) or used in mixture with an active partner (ie. fluoxapyroxad + pyraclostrobin, fluopyram + trifloxystrobin, etc.) that allows the product to be labeled for the disease but does not provide a truly robust resistance management strategy (and therefore less robust IPM chemical component) for control of this potentially aggressive and destructive disease.

Therefore, products containing benzovindiflupyr (Solatenol® Technology) such as Aprovia and Aprovia Top, are unique in its ability to provide efficacy and relevant selection pressure via an alternate mode of action to that of strobilurin or triazole chemistry. Despite several other SDHI fungicide-containing mixtures labeled for this disease currently in the market, research has shown that it is the partner fungicide, and not the SDHI, that is providing the efficacy of anthracnose on curcurbits and peppers**.** Therefore, benzovindiflupyr provides a unique and powerful tool to ensure optimal management of this disease while ensuring the best and most sustainable chemical control option that fits best with a robust IPM program for control of *Colletotrichum spp*.

In summary, Aprovia Top, containing benzovindiflupyr plus difenoconazole, provides the most active or only active SDHI against the pathogens responsible for anthracnose disease in cucumber, watermelon, squash and peppers (bell and non-bell). Additionally, benzovindiflupyr is highly lipophilic which ensures high intrinsic activity to the target enzyme in the pathogen as well as strong adherence to the leaf waxes allowing for long-lasting efficacy, making Aprovia Top an ideal rotational partner for IPM programs designed to increase efficiency of pesticide use and best manage anthracnose disease in these important crops.

Figure 1. Fontelis label (penthiopyrad): note that while the label includes many diseases of cucurbits, it does not include anthracnose caused by *Colletotrichum spp*. This supports third-party research that penthiopyrad is not active on the relevant species of Colletotrichum that infect cucurbits such as cucumber, watermelon and squash. On pepper, the disease is only listed as suppression and only at the very high rate of 24 oz / Acre.

Crop/Crop Group	Target Diseases	Use Rate per Acre (fl oz)	Remarks
Cucurbit Vegetable (Crop Group 9) Chayote (fruit); Chinese waxgourd (Chinese preserving melon); citron melon; cucumber (field and greenhouse); gherkin (field and greenhouse); gourd, edible (includes hyotan, cucuzza, hechima, Chinese okra); *Momordica* spp. (includes balsam apple, balsam pear, bittermelon, Chinese cucumber); muskmelon (includes cantaloupe - other examples in footnote (1)); pumpkin; squash, summer (field and greenhouse); squash, winter (includes butternut squash, calabaza, hubbard squash, acorn squash, spaghetti squash); watermelon	Alternaria leaf spot and blight* (*Alternaria* spp.) Gray mold* (*Botrytis cinerea*) Gummy stem blight* (*Didymella bryoniae*) Powdery mildew (*Sphaerotheca fuliginea, Erysiphe cichoracearum*)	12 to 16 fl oz	Begin applications prior to disease development and continue on a 5- to 14-day interval. Use higher rate and shorter interval when disease pressure is high. For disease control in greenhouse cucurbits, use FONTELIS® at a rate range of 0.375 - 0.5 fl oz of product (0.75 - 1 tablespoon) per gallon of spray per 1360 sq ft. These rates equal field rates of 12-16 fl oz/acre.
	Sclerotinia stem rot* (*Sclerotinia sclerotiorum*)	16 fl oz	
Make no more than 2 sequential applications of FONTELIS® fungicide before switching to a fungicide with a different mode of action. For control of Gummy stem blight where Group 7 fungicide resistance is suspected, tank mix FONTELIS® with a minimum of 1.5 lb active chlorothalonil/acre. Minimum time from application to harvest (PHI) is 1 day. Do not exceed 67 fl oz (0.87 lb active ingredient)/acre per year.			

(1) Muskmelon: includes true cantaloupe, cantaloupe, casaba, Santa Claus melon, crenshaw melon, honeydew melon, honey balls, Persian melon, golden pershaw melon, mango melon, pineapple melon, snake melon, and other varieties and/or hybrids of these.
*Not for use in California

Crop/Crop Group	Target Diseases	Use Rate per Acre (fl oz)	Remarks
Fruiting Vegetable (Crop Group 8-10) African eggplant; bush tomato; bell pepper (field and greenhouse); cocona; currant tomato; eggplant; garden huckleberry; goji berry; groundcherry; martynia; naranjilla; okra; pea eggplant; pepino; nonbell pepper (field and greenhouse); roselle; scarlet eggplant; sunberry; tomatillo; tomato (field and greenhouse); tree tomato	Alternaria blights and leaf spots (*Alternaria* spp.) Black mold (*Alternaria alternata*) Early blight (*Alternaria solani*) Gray mold* (*Botrytis cinerea*) Powdery mildew (*Leveillula taurica*) Basal Stem Rot (*Sclerotium rolfsii*) Septoria leaf spot* (*Septoria* spp.) Target spot (*Corynespora cassiicola*)	16 to 24 fl oz	Begin applications prior to disease development and continue on a 7- to 14-day interval. Use higher rate and shorter interval when disease pressure is high. For disease control in greenhouse peppers and tomatoes, use FONTELIS® at a rate range of 0.5 - 0.75 fl oz of product (1 - 1.5 tablespoons) per gallon of spray per 1360 sq ft. These rates equal field rates of 16-24 fl oz/acre. Basal Stem Rot: apply initial application as a directed spray to the base of the tomato plant, 5-10 days after transplanting. Follow with a second application 14 days later. Continue applications with an effective fungicide with a different mode of action.
	Disease suppression: Anthracnose (*Colletotrichum* spp.)	24 fl oz	
Tomatoes	**Soil-borne Diseases** Rhizoctonia seedling blight/rot (*Rhizoctonia spp*) Southern blight (*Sclerotium rolfsii*)	1.0 - 1.6 fl oz/ 1000 row-ft	Make at-plant, pre-plant incorporated, in-furrow, transplant drench, or drip applications. Maximum rate per acre per application is 24 fl oz. See soil-borne disease section instructions.
Make no more than 2 sequential applications of FONTELIS® before switching to a fungicide with a different mode of action. Minimum time from application to harvest (PHI) is 0 days. Do not exceed 72 fl oz (0.94 lb active ingredient)/acre per year in total from any combination of soil and foliar treatments.			

*Not for use in California

Figure 2. SDHI fungicide introductions: Although SDHI fungicides have been in the market for several decades, only since the 2000s has this class of chemistry become more widespread. Most of the recent introductions since 2010 are comprised of the more modern 'pyrazole carboxamides', however, most of these that are labeled on cucurbits and peppers are not active on *Colletotrichum spp*. and are therefore used in mixture with an active QoI or triazole DMI partner.

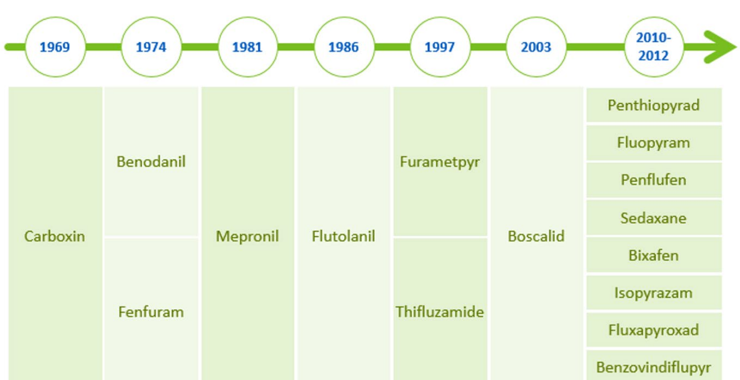
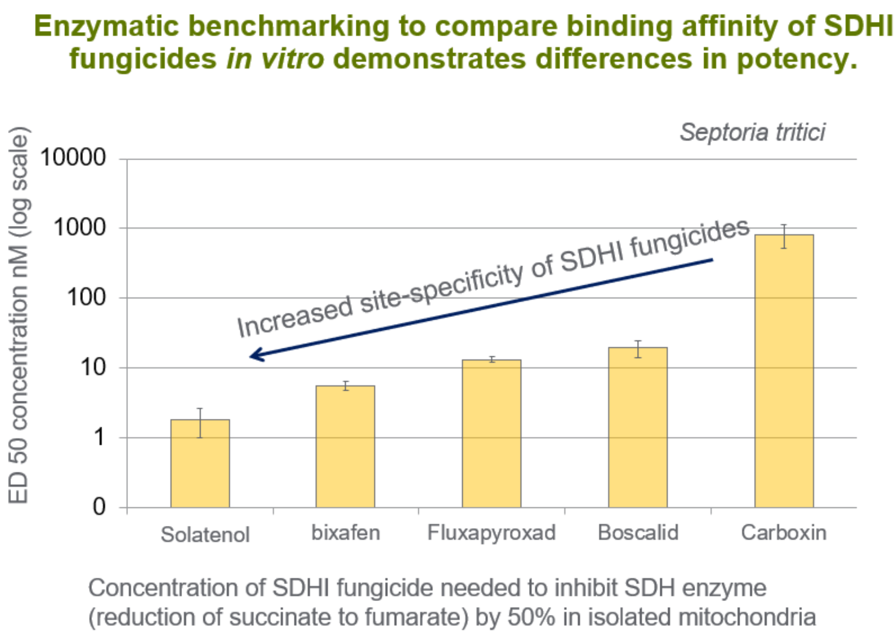
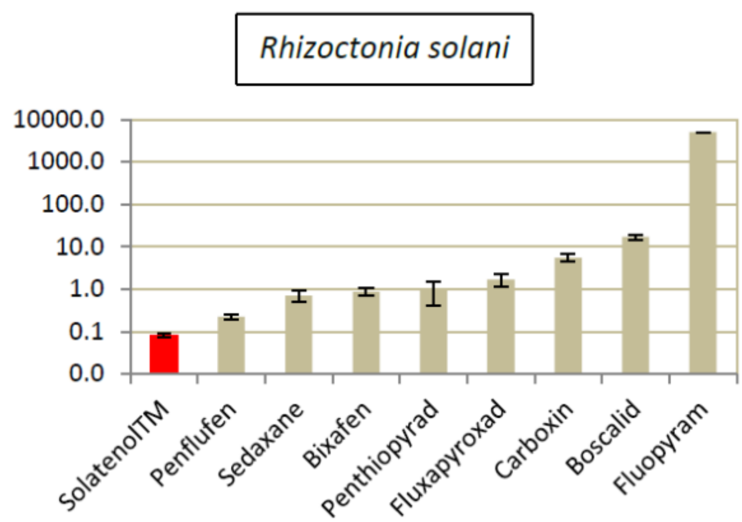


Figure 3. Enzymatic benchmarking: Solatenol has increased site-specificity (intrinsic activity) to the SDH target enzyme in both ascomycetes (A) and basidiomycetes (B) compared to other SDHI fungicides (note logarithmic scale). Syngenta in-house experiments, Jealott's Hill, UK, 2010.

(A)



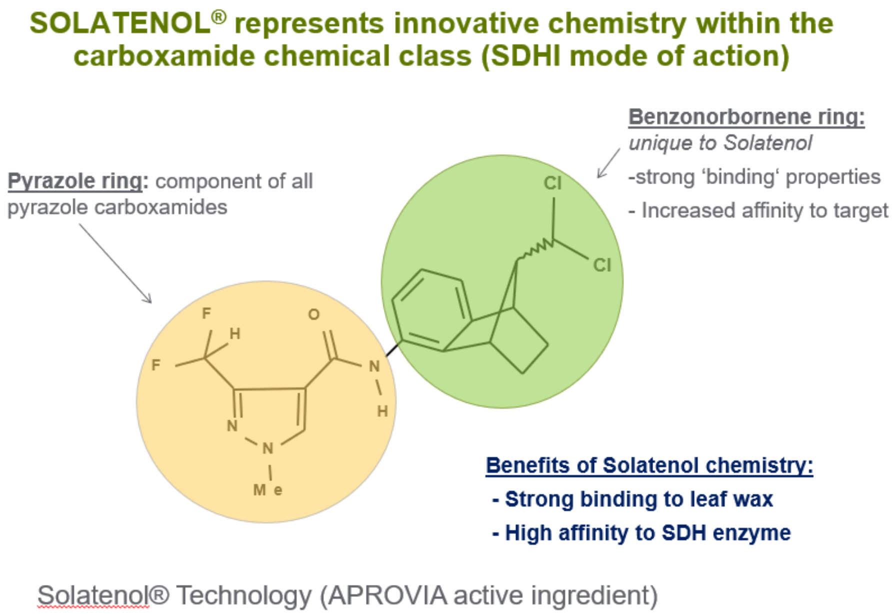
(B)



Enzymatic benchmarking demonstrates the lowest concentration (nM) to inhibit the SDH enzyme by 50% (benefits document, EPA MRID No. 49557601). Therefore, at a lower rate, benzovindiflupyr is more effective than other active ingredients of the same mode of action for Rhizoctonia control.

Figure 4. **Benzovindiflupry molecule**, contains a unique molecular structure that makes the fungicide more lipophillic (A) which results in high affinity to both the target enzyme in the pathogen as well as to the wax layer of leaves (B)

(A)



(B) Affinity and accumulation of benzovindiflupyr in a soybean leaf over 28 days demonstrates higher levels within the waxes of the leaf, which provides more persistence and long-lasting efficacy than penthiopyrad, bixafen, fluopyram (data not shown) and fluxapyroxad (data not shown). The same partitioning trends have been observed on cucumber, grape and tomato leaves (data not shown).

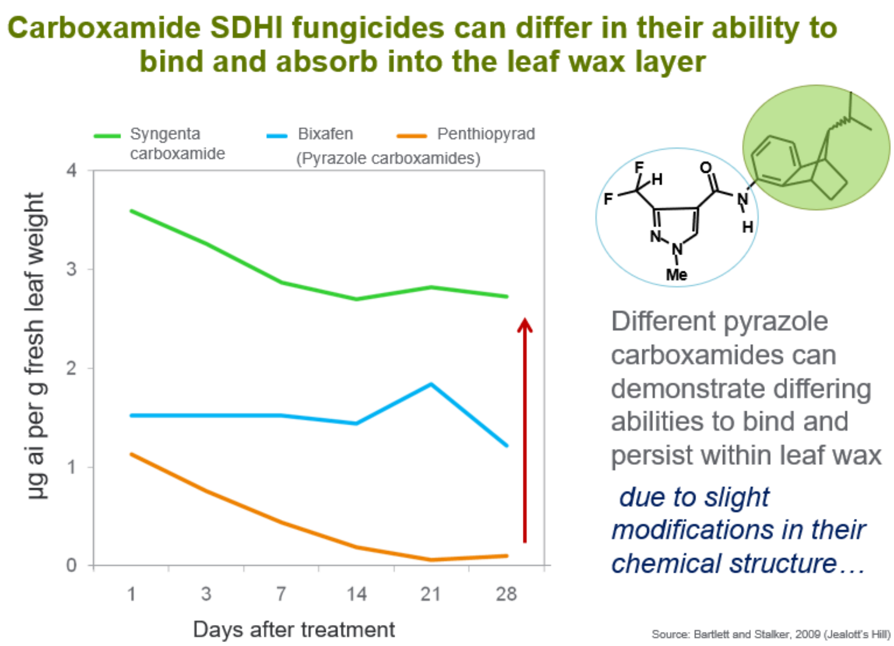


Figure 5. The Group 7 SDHI mode of action is represented by a diverse class of chemistry. The pyrazole-4-carboxamides, which include benzovindiflupyr, are among the most potent and widespread fungicides in the market, although the pathogen spectrum is quite variable among the fungicides. Benzovindiflupyr has been identified as the most active on *Colletotrichum spp*., including *C. orbiculare*, causing cucurbit anthracnose and *C. acutatum* and *C. gloeosporioides*, causing pepper anthracnose.

MOA	TARGET SITE AND CODE	GROUP NAME	CHEMICAL OR BIOLOGICAL 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		
		Quinazoline	quinazoline	fenazaquin		
	C2 complex II: succinate-dehydrogenase	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		
			phenyl-cyclobutyl-pyridineamide	cyclobutrifluram		
			furan- carboxamides	fenfuram		
			oxathiin-carboxamides	carboxin oxycarboxin		
			thiazole-carboxamides	thifluzamide		
			pyrazole-4-carboxamides	benzovindiflupyr bixafen fluindapyr fluxapyroxad furametpyr inpyrfluxam isopyrazam penflufen penthiopyrad sedaxane		
			N-cyclopropyl-N-benzyl-pyrazole-carboxamides	isoflucypram		
			N-methoxy-(phenyl-ethyl)-pyrazole-carboxamides	pydiflumetofen		
			pyridine-carboxamides	boscalid		
			pyrazine-carboxamides	pyraziflumid		

Figure 6. Research papers comparing SDHI efficacy to Colletotrichum species, A) and screen clips of relevant data or conclusions, B). Of all the SDHI's labeled on cucurbits and peppers, only benzovindiflupyr has sufficient efficacy on Colletotrichum spp., including *C. orbiculare*, *C. acuatum*, and *C. gloeosporioides*. Links to journal articles: https://pubmed.ncbi.nlm.nih.gov/26732510/; https://pubmed.ncbi.nlm.nih.gov/35249649/ . For some species of Colletotrichum, penthiopyrad has some activity but is not labeled for cucurbit anthracnose and claims suppression only for pepper anthracnose. All other SDHI fungicides rely on the mix partner for control, despite high levels of QoI resistance to *Colletotrichum spp*.

(A)

Research Article SCI

Received: 30 September 2015 Revised: 27 December 2015 Accepted article published: 6 January 2016 Published online in Wiley Online Library: 9 February 2016

(wileyonlinelibrary.com) DOI 10.1002/ps.4216

Efficacy of SDHI fungicides, including benzovindiflupyr, against *Colletotrichum* species

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Abstract

BACKGROUND: *Colletotrichum* species cause anthracnose diseases on many plants and crops. A new generation of succinate dehydrogenase inhibitors (SDHIs) was developed recently. The inhibitory activity of the five SDHI fungicides against *Colletotrichum* species was determined in this study.

RESULTS: Isolates of *C. gloeosporioides*, *C. acutatum*, *C. cereale* and *C. orbiculare* were insensitive (naturally resistant) to boscalid, fluxapyroxad and fluopyram on YBA agar medium. In contrast, these isolates were relatively sensitive to penthiopyrad, except for *C. orbiculare*. Most interestingly, benzovindiflupyr showed highest inhibitory activity against all of these four species. Benzovindiflupyr was effective against *C. gloeosporioides* and *C. acutatum* on apple and peach fruit, as well as on cucumber plants inoculated with *C. orbiculare*. The *sdhB*, *sdhC* and *sdhD* genes encoding the subunits of fungicide-targeted succinate dehydrogenase were sequenced, but, despite high polymorphisms, no apparent resistance mutations were found in *Colletotrichum* species.

CONCLUSIONS: This is the first report on the activity of benzovindiflupyr against *Colletotrichum* species. The broad-spectrum efficacy of benzovindiflupyr within the *Colletotrichum* genus might be exploited when designing disease management strategies against various pathogens on a wide range of crops. Other mechanism(s) than fungicide target-site modification may be responsible for differential sensitivity of *Colletotrichum* species to SDHI fungicides.

(B)

Table 4. Sensitivity of *Colletotrichum* species isolates to SDHI fungicides (conidial germ tube growth)

Fungicide	Concentration ($\mu g\ mL^{-1}$)	Species[a] and isolate: *C. g.* 5-2-1	*C.a.* GC2-1	*C. c.* S0133[b]	*C. o.* CL-2
Boscalid	100	+++[c]	+++	+++	+++
Fluxapyroxad	100	+++	++	NT	++
Penthiopyrad	100	++	++	++	+++
Fluopyram	100	++	++	NT	+++
Benzovindiflupyr	1	+	+	−	−
Benzovindiflupyr	0.1	+	+	−	− − +
None		+++	+++	+++	+++

[a] *C. g.*, *C. gloeosporioides*; *C. a.*, *C. acutatum*; *C. c.*, *C. cereale*; *C. o.*, *C. orbiculare*.
[b] = MAFF306613.
[c] −, no growth; +, 1−3 × length of conidium; ++, 3−10 × length of conidium; +++, >10 × length of conidium.

Table 5. Suppressive activity of SDHI fungicides against *Colletotrichum* species isolates on detached apple fruit

Species[a]	Isolate	Disease suppression (%) – Fungicide: Boscalid	Fluxapyroxad	Penthiopyrad	Fluopyram	Benzovindiflupyr
C. g.	5-2-1	−1.3 b[b]	2.0 b	11.9 b	3.8 b	40.0 a
C. a.	GC2-1	−43.2 b	−20.7 b	82.8 a	−14.9 b	60.6 a

[a] *C. g.*, *C. gloeosporioides*; *C. a.*, *C. acutatum*.
[b] A Brown−Forsythe test was conducted to assess the equality of variance between experiments. Least significant difference (LSD) tests were conducted at $P = 0.05$. The same letters indicate no significant difference.

3.4 Suppressive activity of SDHI fungicides against *C. orbiculare* isolates on cucumber plants

Spray applications of benzovindiflupyr at 100 mg L^{-1} effectively suppressed anthracnose disease on intact cucumber plants inoculated with *C. orbiculare* (Fig. 1). However, the efficacy of boscalid at 334 mg L^{-1} and penthiopyrad at 100 mg L^{-1} was very poor. Disease suppression was 96.7, 20.0 and 21.6% on average, respectively, after treatment with benzovindiflupyr, boscalid and penthiopyrad (Table 7).

Benzovindiflupyr applied at 100 mg AI L^{-1} suppressed the development of disease caused by *C. gloeosporioides* and *C. acutatum* on apple and peach fruit in inoculation tests. In addition, when benzovindiflupyr was sprayed at 100 mg AI L^{-1} prior to pathogen inoculation, this fungicide showed high control efficacy against anthracnose disease on cucumber. Although field trials still need to be done for confirmation, the broad-spectrum fungicide benzovindiflupyr seems to be promising and attractive either as a solo product or in combination with other fungicides for the control of diseases such as apple bitter rot, grapevine ripe rot and strawberry anthracnose caused by *Colletotrichum* species, in addition to other major diseases. As briefly reported recently,[25,42] boscalid-resistant isolates of *B. cinerea* showed high sensitivity to benzovindiflupyr in conidial germination tests conducted on YBA agar medium, irrespective of mutation types (H272R/Y and N230I) in their *sdhB* gene. Furthermore, all isolates of *A. alternata* resistant to boscalid showed sensitivity to benzovindiflupyr, irrespective of mutation types in the *sdh* subunit genes so far tested. Thus, the superior activity of benzovindiflupyr against *Colletotrichum* species compared with older SDHI fungicides might be exploited when designing disease management strategies in a wide range of crops.

(A)

Sensitivity to fungicides in isolates of *Colletotrichum gloeosporioides* and *C. acutatum* species complexes and efficacy against anthracnose diseases

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ARTICLE INFO

Keywords:
Anthracnose
Benzovindiflupyr
Colletotrichum acutatum
Colletotrichum gloeosporioides
Mefentrifluconazole
QoI fungicides

ABSTRACT

Colletotrichum species cause diseases on many plants and are among the 'top 10' fungal plant pathogens. Species of the *C. gloeosporioides* and *C. acutatum* complexes are particularly important because they infect temperate fruit crops, but their control relies largely on chemical fungicides. In this study, differences in intrinsic fungicide sensitivity were determined *in vitro* using isolates of the *C. gloeosporioides* sp. complex (*C. fructicola*, *C. siamense*, and *C. tropicale*) and the *C. acutatum* sp. complex (*C. fioriniae* and *C. nymphaeae*), which had never been exposed to fungicides. Mycelial growth of all isolates was sensitive to the QoI azoxystrobin, the SDHI benzovindiflupyr, and the new DMI fungicide mefentrifluconazole. The isolates of *C. nymphaeae* were highly sensitive to the phenylpyrrole fungicide fludioxonil. The isolates of *C. gloeosporioides* sp. complex were sensitive to the bisguanidine fungicide iminoctadine-albesilate, whereas those of *C. acutatum* sp. complex were inherently insensitive. These results are valuable when sensitivity of field populations is monitored in resistance management. Although SDHI fungicides are largely not effective against diseases caused by *Colletotrichum* species, benzovindiflupyr controlled anthracnose disease of various crops such as kidney bean, garland chrysanthemum, and strawberry, caused by *C. lindemuthianum*, *C. chrysanthemi*, and *C. siamense*, respectively, demonstrating this fungicide to be unique among SDHIs and having a broad control spectrum against anthracnose. To help understanding the reason for differential activity of benzovindiflupyr and boscalid, *sdhB* gene sequences were analyzed but those of *C. lindemuthianum*, *C. chrysanthemi*, and *C. scovillei* revealed no known mutations reported to be responsible for SDHI resistance in other fungi, indicating that other mechanism(s) than target-site modification may be involved in differential sensitivity to benzovindiflupyr and boscalid, found in *Colletotrichum* species.

A)
https://www.apsnet.org/meetings/annual/meetingarchives/planthealth2019/Documents/Abstracts/aps2019ab389.htm

B)

plant health 2019

APS ANNUAL MEETING

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POSTERS: Chemical control

Efficacy and baseline of succinate dehydrogenase inhibitor (SDHI) fungicides for management of Colletotrichum crown rot of strawberries

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The current management of Colletotrichum crown rot (CCR) of strawberry, caused by *Colletotrichum gloeosporioides*, relies on the use of a few fungicide classes. Since resistance to QoI fungicides was recently detected, alternative fungicide groups are needed to control the disease. Our objective was to evaluate the efficacy of succinate dehydrogenase inhibitor (SDHI) fungicides in managing CCR. Twenty-plant plots of cultivar Strawberry Festival were inoculated 4 weeks after planting. Five SDHI fungicides, fluopyram, isofetamid, penthiopyrad, fluxapyroxad, and benzovindiflupyr, were either applied 2 days before or one day after inoculation (DAI). SDHI treatments were compared with a non-treated control and with the most common fungicides used on CCR management, i.e. thiophanate-methyl, pyraclostrobin, and captan. CCR incidence was evaluated once a week by counting the number of wilted and dead plants. Benzovindiflupyr applied 1 DAI was effective in reducing plant mortality and disease development. Captan was the most effective when applied preventively. The baseline of 100 *C. gloeosporioides* isolates was determined in vitro using a spiral gradient dilution assay. The EC_{50} for benzovindiflypyr and penthiopyrad varied from 0.08-1.11 and 0.45-3.17 µg/mL, respectively, whereas the other SDHI fungicides did not inhibit fungal growth. Our results indicate that benzovindiflupyr could serve as an alternative to manage CCR in Florida if the product is registered.

A)
https://content.ces.ncsu.edu/anthracnose-of-pepper

B)

Note that only benzovidiflupyr is listed as 'E' for excellent cotnrol of pepper anthracnose, while pyraclostrobin is likely the active partner in Priaxor (based on reports in the literature referenced above, fluxapyraxoad will not inhibit growth of C. actuatum in petri dishes), however, QoI resistance risk is higher when not protected by another active product. Fluopyram + trifloxystrobin is rated 'G' for good, however, solo trifloxystrobin (which provides a higher load of the active) is rated 'E', implying that the carboxamide is not adding much or any efficacy. Penthiopyrad is rated 'G', but only has suppression on the label. This data supports the laboratory results that benzovidiflupyr is much more active on Colletotrichum spp., than other SDHI's labeled for this pathogen. Penthiopyrad (Fontelis) is not labeled for cucurbit anthracnose.

Table 1. List of fungicides labeled for management of anthracnose on pepper plants.

Active Ingredient	Example Product[1]	FRAC[2]	Efficacy[3]
Azoxystrobin	Various	11	E
Azoxystrobin + difenoconazole	Quadris Top	11 + 3	E
Chlorothalonil	Various	M05	F
Chlorothalonil + cymoxanil	Ariston	M05 + 27	F
Difenoconazole + benzovindiflupyr	Aprovia Top	11 + 3	E
Famoxadone + cymoxanil	Tanos	11 + 27	F
Fluopyram + trifloxystrobin	Luna Sensation	7 + 11	G
Mancozeb	Various	M03	F-G
Mancozeb + copper	ManKocide	M03 + M01	F-G
Penthiopyrad	Fontelis	7	G
Pyraclostrobin	Cabrio	11	E
Pyraclostrobin + fluxapyroxad	Priaxor	11 + 7	E
Trifloxystrobin	Flint	11	E

[1] Other products on the market will have the same active ingredient(s). Always read fungicide labels before application.
[2] FRAC code (Fungicide Resistance Action Committee code). Avoid using products with the same FRAC code in consecutive or mixed applications to minimize the development of resistant populations. For more information, visit frac.info.
[3] Efficacy ratings: E = excellent; G = good; F = fair; P = poor

GINSENG
Meets Criteria III and IV – Resistance management and IPM.
Target pest: *Alternaria panax*

Fungal disease management on ginseng requires intensive use of fungicides and other cultural practices to ensure high quality, commercially acceptable production of ginseng. Most of the ginseng grown in the US for commercial production is grown in Wisconsin and Michigan, with some limited production in Ohio and other northern states. (Wild ginseng also occurs in mostly mountainous areas of Appalachia throughout the central and northeast United States). The key diseases of ginseng are powdery mildew caused by *Erisyphe spp*. and Alternaria blight caused by *Alternaria panax*. Secondary pathogens included *Botrytis cinerea*, *Phytophthora cactorum*, *Rhizoctonia solani*, and *Cylindocarpon destructans*. The most economically important fungal pathogen and the target of most fungicide research in ginseng is *Alternaria panax* (**figure 1**).

Traditionally, very few fungicide products were labeled for use in ginseng. This is most likely due to the investment required to bring new products on relatively small crops like ginseng. However, over the last decade or so, IR-4 has worked closely with the pesticide manufacturers, the ginseng industry and the EPA to help bring new fungicide solutions to the market for use on ginseng and today there are numerous products that are labeled. That said, in order to have a robust IPM program which consists of both cultural and chemical practice, a good portfolio of fungicide products is required to ensure good rotational opportunities, minimize the risk of pest resistance, and ensure a high-quality, disease-free crop for years to come. Without the use of modern and diverse fungicides, ginseng production and robust IPM programs would be significantly compromised in the USA.
https://pesticideguy.org/2014/09/11/american-ginseng-production-would-be-devastated-without-fungicides/

Alternaria spp. is a common pathogen across a wide range of crops, and unfortunately, is very prone to resistance. Iprodione was an effective fungicide for Alternaria control in ginseng in the 1980s, and at the time was one of the sole fungicides registered to control Alternaria. After only three seasons of use, resistance to iprodione was reported and is no longer an effective tool for controlling *Alternaria spp*. on ginseng (*Rahimain, M.K., Resistance of* Alternaria panax *to iprodione under field conditions, Phytopathology 77:1747-1747 (1987)).* Many reports of Alternaria resistance have occurred on other crops like tomatoes and potatoes to both QoI and SDHI chemistry (*Tymon L., and D.A. Johnson, Fungicide resistance of two species of Alternaria from potato in the Columbian Basin of Washington, Plant Disease 98:1648-1653 (2014)* https://apsjournals.apsnet.org/doi/pdf/10.1094/PDIS-12-13-1199-RE). Therefore, it is very important to have fungicide options that contain multiple modes of action to help manage resistance to diseases caused by *Alternaria spp*.

Benzovindiflupyr is a pyrazole carboxamide SDHI that is highly effective on many leaf spot pathogens, including *Alternaria spp*. Although the Fungicide Resistance Action Committee (or FRAC) has designated the chemistry as 'medium to high risk' (www.frac.info), the full resistance risk to any given fungal disease also depends on agronomic practice (ie. proper fungicide rotation or mixture, using labeled rates, crop rotation, removal of crop debris, etc.) as well as the pathogen risk. Some pathogens are more prone to resistance than others. For example, resistance reports of *Alternaria spp*. and *Botytis* *spp*. are much more widespread than pathogens such as *Rhizoctonia spp*., *Sclerotinia spp*., and certain basidiomycetes such as the *Sclerotium rolfsi* and the rusts (although nearly all pathogens can become resistant under conducive conditions). In the case of *Alternaria panax* on ginseng, it will be very important to ensure a wide range of fungicide products to help manage the development of resistance, as well as supporting a good IPM program for disease management in ginseng. To ensure a robust IPM strategy on ginseng, it is important to consider the following agronomic approaches: 1) ensuring disease-free seed, 2) quality crop rotation with non-host crops in a two-to-three year rotation, 3) sanitation practices to remove or destroy crop residue that could harbor pest inoculum, 4) the use of pest-resistant varieties, and 5) the use of effective fungicide chemistries in combination with 1 – 4 above. No one single use of these practices can be successfully utilized to completely control this highly aggressive disease under conducive environmental conditions, therefore, a combination of these practices (IPM approach) is required to successfully combat this disease and maintain yields that ensure marketability of unblemished and high-quality ginseng production. The use of effective chemistry is extremely important to any successful IPM program and having choices of different products and product combinations (including premix fungicide products) is key to managing resistance and ensuring optimal disease management in ginseng.

Many of the SDHI fungicides now labeled in ginseng are more recent product offerings available for control of Alternaria. These fungicides are (the SDHI component is underlined) Luna Sensation (<u>fluopyram</u> + trifloxystrobin), Merivon SC (<u>fluxapyroxad</u> + pyraclostrobin), Endura (<u>boscalid</u>) and Fontelis (<u>penthiopyrad</u>), and most recently, Aprovia Top (benzovinidflupry + difenoconazole). Although these SDHI fungicides are within the same mode of action and technically considered 'cross-resistant' according to FRAC, we do know that some mutations do not confer full insensitivity across all SDHI's. It is well documented in the literature that many boscalid-resistant strains of Alternaria spp. are still controlled by many of the newer pyrazole carboxamide SDHI fungicides (Landschoot, et. al,. Boscalid-resistance in *Alternaria alternata* and *Alternaria solani* populations: An emerging problem in Europe. Crop Protection 92: 49 – 59 (2017): (https://www.sciencedirect.com/science/article/pii/S0261219416302897). In Syngenta, our research to understand and explore the evaluation of Boscalid resistant mutants of *Alternaria solani* demonstrated that some mutations are more cross-resistant than others, and that two of the more common SDHI mutations in *Alternaria spp*., sdhB-H227R and sdhB-H277Y, that cause complete insensitivity to Bocalid are still inhibited by benzovindiflupyr based on EC50 calculations of mycelial growth in petri dish studies. This confirms that cross-resistance, while correct to conservatively classify across all SDHI fungicides, is in fact, partial for many of the mutations (**figure 2**).

The registration of Aprovia Top (benzovindiflupyr + difenoconazole) was done in collaboration with the IR-4 project, with the intention of providing more and effective tools for ginseng growers. Data collected by IR-4 and used to determine efficacy of the product are provided below (**Figure 3**). Aprovia Top is among the highest rated performer in these trials and shows good promise to control *Alternaria panax*. Furthermore, the other SDHI-containing products currently labeled on ginseng are either solo SDHI product or in mixture with a QoI product (despite being tested in trials, Luna Experience is not labeled on ginseng, the product labeled is Luna Sensation, which contains SDHI + QoI fungicide), and therefore, **Aprovia Top offers the only premix SDHI fungicide used in mixture with a triazole, providing both a potent SDHI component for control of the pathogen and in mixture with a lower resistance-risk**

partner that is less prone to fungicide resistance to this pathogen. This combination not only provides more ideal concept in terms of fungicide resistance management but has increased value as a product to be used in an IPM strategy that requires rotation with other modes of action. In addition, in comparison to fluopyram, the amount of SDHI active ingredient in Aprovia Top is roughly half of what is required of fluopyram in the labeled rate of Luna Sensation, 75 gai/ha versus 140 gai/ha, respectively (**Figure 4**). A more efficient use of pesticide chemistry is an important part of a robust IPM strategy.

In addition, since registration on ginseng the ability of benzovindiflupyr has been evaluated on many of the secondary diseases, such as Cylindocarpon, which can result in plant death. In a trial program to evaluate performance, benzovindiflupyr did provide performance which could offer further opportunities for Aprovia Top on ginseng (**Figure 5**).

In conclusion, as ginseng requires multiple fungicide applications for robust disease control, particularly for control of *Alternaria spp*., combined with an overall IPM strategy as described above, new fungicides that will offer value in terms of improved efficacy or a more efficient use of chemistry, a new mode of action, or a novel premix concept would contribute significantly to a robust IPM strategy and be an asset to ginseng growers. Aprovia Top, containing benzovindiflupyr and difenoconzole, provides a highly active SDHI fungicide (that has been shown to control some boscalid and penthiopyrad-resistant isolates of *Alternaria spp*., likely due to enhanced potency) that remains the only labeled SDHI product in premixture with difenoconazole, a triazole fungicide with lower resistance risk than the strobilurin chemistry. Like this, Aprovia Top fungicide is an important addition to the management tools ginseng growers can utilize to ensure a robust IPM program and maintain resistance management practice for controlling Alternaria blight.

Figure 1. Alternaria blight on ginseng, caused by *Alternaria panax*. The disease causes damaging defoliation and is highly destructive to ginseng yield and quality.

Figure 2. Inhibition of wild-type and four SDHI mutants of *Alternaria solani* to three SDHI fungicides. BOS = boscalid, PENT = penthiopyrad, and STL = benzovindiflupyr (also known as Solatenol® Technology). Note that benzovindiflupyr (STL) can effectively inhibit growth and demonstrate fungicidal activity to all four mutations that have rendered boscalid completely ineffective, and three of the four ineffective for penthiopyrad, in comparison to the wild-type. Any inhibition under 10 mg active ingredient / L is likely to provide commercial levels of disease control. Over 10 mg will result in poor field performance and = or > 100 mg is complete loss of efficacy. This confirms, depending on mutation, that isolates resistant to boscalid and / or penthiopyrad might still be controlled by benzovindiflupyr, likely due to higher overall potency, or due to partial cross-resistance for some mutations.

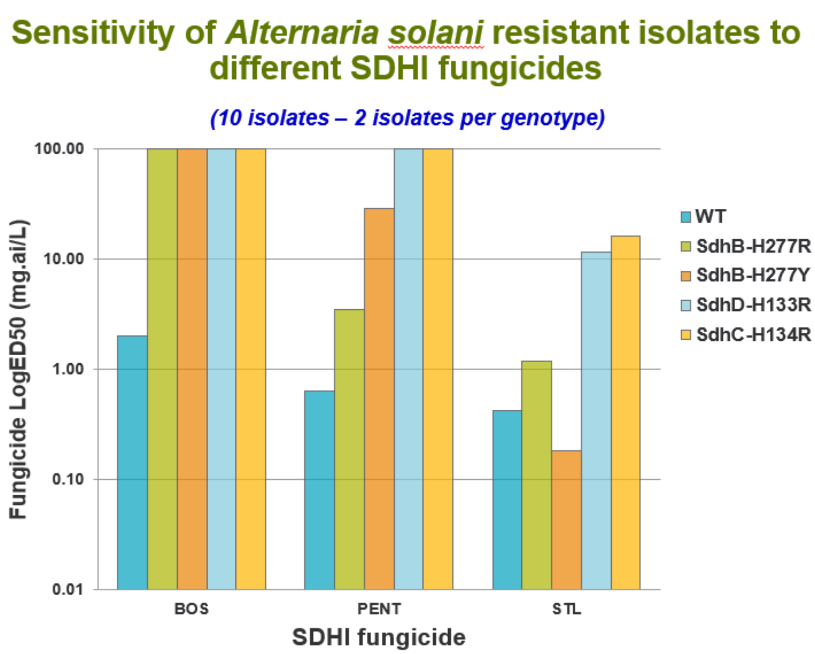

Figure 3. Reports supporting the efficacy of Aprovia Top on ginseng. Note that Aprovia Top is one of the most effective products for control of Alternaria blight and offers a highly active SDHI fungicide and triazole chemistry in a premixture, and does not include the typically higher resistance-risk QoI fungicides, known for contributing to widespread resistance among *Alternaria spp.* pathogens.

Evaluation of New Fungicides to Control of Alternaria Blight In a Two-Year-Old Ginseng Garden

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Objective: Evaluation of new fungicides, biological control agents and combinations of biological control agents with known effective products for the ability to control Alternaria blight in a two-year-old ginseng garden.

Background: Applications made 50 gallons/acre using a CO_2 backpack sprayer with a boom equipped with four 8003 flat fan nozzles spaced 18 inches apart operating at 36 psi. Sprays were initiated May 21 and were reapplied at 7-day intervals.

Treatment	Active Ingredient	Company	Rate 50 gal/Acre	Disease Severity* 8/18
Untreated Control				**8.7**
Endura	boscalid	BASF	4.5 oz	**6.0**
Luna Experience	fluopyram + tebuconazole	Bayer	12 fl oz	**2.5**
Luna Sensation	fluopyram + trifloxy.	Bayer	7.6 fl oz	**2.0**
Luna Tranquility	fluopyram + pyrithmenil	Bayer	11.2 fl oz	**7.0**
Luna Privilege	fluopyram	Bayer	2.82 fl oz	**6.9**
GWN-10411	experimental	Gowan	10 fl oz	**4.2**
Aprovia Top	experimental	Syngenta	8.5 fl oz	**2.2**
Thyme Guard	thyme oil	Ag. Res. Int'l	0.25% v/v	**8.3**
Serenade ASO	*Bacillus subtilis*	Bayer	6 qt	**8.9**
PreStop	*Gliocladium catenulatum*	Ag Bio Inc	1000 g	**8.5**
Endura 70 WG + Bravo alt. Thyme Guard alt. Merivon SC + Dithane DF	boscalid chlorothalonil thyme oil fluxapyroxad + pyraclo. mancozeb	BASF Syngenta Ag. Res. Int'l BASF Loveland	4.5 oz 2 pt 0.25% v/v 5.5 fl oz 2 lb	**4.0**
Endura 70WG + Bravo alt. Serenade ASO alt. Merivon SC + Dithane DF	boscalid chlorothalonil *Bacillus subtilis* fluxapyroxad + pyraclo. mancozeb	BASF Syngenta Bayer BASF Loveland	4.5 oz 2 pt 6 qt 5.5 fl oz 2 lb	**4.9**
Endura 70WG + Bravo alt. Prestop alt. Merivon SC + Dithane DF	boscalid chlorothalonil *Gliocladium catenulatem* fluxapyroxad + pyraclo. mancozeb	BASF Syngenta Ag Bio Inc BASF Loveland	4.5 oz 2 pt 1000 g 5.5 fl oz 2 lb	**4.1**

*Disease severity is 1-10; 1=no disease, 2-9=increased levels of infection, 10=100% defoliation.

Figure 3 (cont):

AMERICAN GINSENG (*Panax quinquefolium*)
Alternaria blight; *Alternaria panax*

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Evaluation of Aprovia Top to control Alternaria blight on four-year-old ginseng, 2016.

This study was conducted at a cooperator's farm in Marathon County, WI on four-year-old ginseng plants grown under 80% shade-cloth. Beds were 4 ft wide with 1 ft between beds. Treatment blocks consisted of a 10-ft bed with a 2-ft buffer on each end. Treatments were replicated six times in a randomized complete block design. Weed control and fertilization were made according to commercial production standards. Fungicides were applied with a CO_2 backpack boom sprayer equipped with four T-Jet 8003VS flat fan nozzles spaced 18 in. apart, operating at 40 psi, and delivering 50 gal/A. All treatments were initiated on 2 Jun. Scala was reapplied at 7-day intervals on 9, 16, 23, 30 Jun and 8, 14, 22, 29 Jul. Aprovia Top was reapplied at 14-day intervals on 16, 30 Jun and 14, 29 Jul. Scanner, a non-ionic surfactant, was added to all fungicide applications at a rate of 3 fl oz/50 gal. The number of plants in each plot with symptoms of *A. panax* infection were counted and a disease severity rating (1-10; 1=no disease, 2-9=increased levels of *A. panax* infection, 10=complete defoliation) was noted on 22 Jun and 7, 19 Jul.

Disease pressure was severe in this trial with the untreated control plots averaging 105.7 plants infected with *A. panax* by the final rating. Alternaria blight spread rapidly in the research plot between the initial fungicide application date of 2 Jun and the 22 Jun rating. Although ratings continued into Jul, few newly infected plants were observed. It should be noted that Scale SC did limit *A. panax* infection compared to the untreated control for all rating dates, however this differences was not statistically significant. Although only a total of two applications were made of Aprovia Top while disease pressure was most severe, the product was highly efficacious and significantly limited Alternaria blight compared to the untreated control for all rating dates. Phytotoxicity was not observed on any of the treated plants in this study.

Treatment and rate/50 gal; *application interval*	Avg. # number infected plants/10 ft			Disease severity*		
	22 Jun	7 Jul	19 Jul	22 Jun	7 Jul	19 Jul
Untreated control	101.7 b**	105.7 b	105.7 b	3.3	4.3 b	4.5 b
Scala SC 18 fl oz + Scanner 3 fl oz; *7-day*	83.2 ab	86.8 b	86.8 b	3.5	3.7 ab	3.7 ab
Aprovia Top 14 fl oz + Scanner 3 fl oz; *14-day*	33.7 a	37.5 a	37.5 a	2.5	2.7 a	2.7 a

*Disease severity rating is 1-10; 1=no disease, 2-9=increased levels of *A. panax* infection, 10=complete defoliation.
**Column means with a letter in common or no letter are not significantly different (Fisher's LSD; P=0.05).

Figure 4. Ginseng labels for Luna Sensation (left) and Aprovia Top (right). The required rate of 7.6 oz / acre of Luna Sensation (0.125 lbs active / acre) delivers 140 gai/ha of active ingredient, whereas the required rate of 13.4 oz of Aprovia Top (0.068 lbs active / acre) – *note the label is calculated for the max of four applications, 0.068 lbs is for a single application* – delivers 75 gai/ha of active ingredient.

Ginseng

Disease Control	Application Rate	Application Instructions
Powdery mildew (*Erysiphe* spp.) Alternaria blight (*Alternaria panax*) Botrytis blight (*Botrytis cinerea*)	7.6 fl oz/acre (0.125 lb/acre fluopyram) (0.125 lb/acre trifloxystrobin)	Apply using ground, aerial, or chemigation equipment. Apply at the critical timings for disease control. Refer to University and/or extension guidelines for best application timings. Continue as needed on a 14-day interval.

Restrictions:
- Maximum single application rate: 7.6 fl oz/acre of LUNA SENSATION (0.125 lb/acre fluopyram and 0.125 lb/acre trifloxystrobin)
- Maximum annual application rate: 15.3 fl oz of LUNA SENSATION per acre (0.251 lb/acre fluopyram and 0.251 lb/acre trifloxystrobin) per year.
- Maximum number of applications per year: 2
- **DO NOT** apply more than 0.446 lbs fluopyram or 0.375 lbs trifloxystrobin per acre per year, including soil and foliar uses, regardless of formulation or method of application.
- **DO NOT** apply LUNA SENSATION within 7 days of harvest.
- To limit the potential for development of disease resistance to these fungicide classes, **DO NOT** make more than 2 sequential applications of LUNA SENSATION or any Group 7 or Group 11 containing fungicide before rotating with a fungicide from a different Group.

7.5 Ginseng

Crops (Including all cultivars, varieties, and/or hybrids of these)
Not for use in California

Ginseng

Target Disease	Rate (fl oz/A)	Application Timing	Use Directions
Ginseng Alternaria blight (*A. panax*) Powdery mildew (*Erysiphe* spp.)	13.5	For foliar disease, make an application at the onset of disease or when conditions are conducive for disease.	Apply by ground. For ground applications, use a minimum of 50 gal/A of water. See **Section 4.4.5**.

Resistance Management:
- Refer to **Section 3.2**.
- For resistance management, make no more than 2 applications before alternating to another fungicide with a non-Group 7 mode of action.

USE RESTRICTIONS

1. Refer to **Section 6.1** for additional product use restrictions.
2. **Maximum Single Application Rate:** 13.5 fl oz/A
3. **Minimum Application Interval:** 14 days
4. **Maximum Annual Rate:** 54 fl oz/A/year
   a. **DO NOT** exceed 0.272 lb ai/A/year of benzovindiflupyr-containing products.
   b. **DO NOT** exceed 0.46 lb ai/A/year of difenoconazole-containing products.
5. **DO NOT** exceed 4 applications per year.
6. **Pre-Harvest Interval (PHI):** 15 days

Figure 5. Benzovindiflupyr (Solatenol® Technology) may offer opportunities to control secondary pathogens of ginseng, such as Cylindocarpon, which could lead to label expansion opportunities in the future, further providing value of Aprovia Top to ginseng growers. Note that Solatenol is active at 75g ai/ha versus penthiopyrad at 234 gai/ha.