UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

August 28, 2019

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Emended-Review of Bayer Crop Science's Request for an Extension of the Exclusive Use Period for Fluopyram (DP#449228, 453613)

FROM: Thomas Harty, Horticulturist
Biological Analysis Branch

THRU: Jonathan Becker acting for
Monisha Kaul, Chief
Biological Analysis Branch
Biological and Economic Analysis Division (7503P)

TO: Aswathy Balan, Risk Manager Reviewer
Registration Division (7505P)

PRODUCT REVIEW PANEL DATE: July 24, 2019

[Note: This document emends Crop Group / Subgroup designations in Table 1.]

SUMMARY

Bayer CropScience LP (2018) petitioned EPA to request, under FIFRA Section 3(c)(1)(F)(ii), the exclusive use period for data supporting the fungicide/nematicide active ingredient, fluopyram, be extended for three years. In Bayer's submission (MRID 50642501 and 50872501), supporting information was submitted for 16 crops. All 16 uses meet the definition of minor use according to the 2017 USDA Census of Agriculture. BEAD evaluated the registrant claims that the minor uses to qualify under criterion I, III, and IV as defined under FIFRA 3 (c)(1)(F)(ii). BEAD did not evaluate criterion II as it is a risked based determination and therefore defers to the Registration Division to determine if registered alternatives to fluopyram pose greater risks to the environment or human health. This document was emended on August 28th, 2019, to properly reflect crop groups/subgroups and representative residue data provided in Table 1 herein.

It was determined that at least nine of the 16 minor use sites satisfied the data exclusivity criteria. The qualifying crops under criterion III include cucumber, cantaloupe or watermelon, pumpkin, strawberry and pistachio. The qualifying crops under criterion IV include sweet potato, broccoli or cauliflower, cabbage, and sweet cherry. Therefore, the request for fluopyram satisfies criteria III and IV for the nine necessary minor uses sites.

BACKGROUND

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides certain data protection rights to data submitters for their registered pesticides. Section 3(c)(1)(F)(i) states that the original data submitter has a 10-year exclusive use period from the date of registration for the data submitted in support of the original registration. The period of exclusive use may be extended one year for each three minor uses registered, up to a total of 3 additional years, if within 7 years of the commencement of the exclusive use period the registrant demonstrates that:

(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*

A minor use is defined in FIFRA Section 2(ll) as the use of a pesticide on an animal, on a commercial agricultural crop or site, or the protection of public health where "*(1) the total U.S. acreage for the crop is less than 300,000 acres, as determined by the Secretary of Agriculture, or (2) the use does not provide sufficient economic incentive to support the initial registration or continuing registration of a pesticide for such use.*"

In the case of crop groupings, FIFRA 3(c)(1)(F)(ii) states that "*the registration of a pesticide for a minor use on a crop grouping . . . shall be considered for one minor use for each representative crop for which data are provided.*" That is, the maximum number of eligible distinct minor uses for a crop group is equal to the number of representative crops for which residue data have been submitted. For instance, if residue data were submitted for lemon and grapefruit as representative crops for citrus, a crop group that contains several minor uses, the data could support multiple minor uses, but a maximum of two uses could support a request for extension of exclusive use. Greenhouse uses are considered separate use sites from field crops in cases where distinct residue data for field-grown crops are submitted to support the registration.

BEAD evaluated whether at least nine use sites submitted in Bayer's package met the statutory requirement for an extension of data exclusivity by verifying that residue trials were submitted on a one-for-one basis with use sites, verifying minor crop acreage, and validating criteria I, III and IV.

REGISTRANT SUBMISSION

The registrant claims that fluopyram satisfies the FIFRA Section 3(c)(1)(F)(ii) requirements for the following 16 use sites: sweet potato, broccoli, cabbage, cantaloupe, pumpkin, strawberry, peach, cauliflower, cucumber, grapefruit, pistachio, watermelon, lemon, tangerines, apricot, and sweet cherry (Bayer 2018). The registrant claims all uses are associated with a residue trial, are grown on less than 300,000 acres, and are associated with either criteria I and III and/or IV. The registrant package (Bayer 2018) summarized 16 potentially eligible use sites. After an initial

evaluation of the submission the Agency requested Bayer provide additional supplementary material and received an amended submission on July 8th, 2019 (See Bayer 2019; MRID 50872501).

BEAD Analysis

BEAD first confirms that residue trial data is sufficient such that there is a one-for-one relationship to each use site. Then BEAD confirms that each crop meets the definition of a minor crop per FIFRA Section 2(ll)(1) of having less than 300,000 acres grown annually. Finally, BEAD evaluates the biological benefits submitted by the registrant to determine if criteria I, II and/or IV are met. Of the 16 crops listed in the registrant submission, all are supported by residue data (Table 1). However, in the case of cucurbits and brassica crops the registrant proposed more minor use sites than supporting representative crop residue data provided; therefore, only a portion of the minor uses the registrant put forward from the cucurbit and brassica crop groups are eligible. Bayer may claim up to 14 minor use sites if all use sites are cultivated on fewer than 300,000 acres and criteria II, III and/or IV are met.

Table 1. Proposed crops and representative residue data

Crop Group/ Subgroup	**Date, Residue Trial(s)**	**Crop Data Submitted [1]**	**Minor Use Represented [2]**	**Applicable Rep. Crop Limitations**
Root and Tuber Vegetables (1C)	3/2/2016 (49242804)	Potato	Sweet Potato	None
Brassica Vegetable (5A)	3/2/2016 (47567025)	Broccoli	Broccoli	Broccoli or Cauliflower
Brassica Vegetable (5A)	3/2/2016 (47567025)	Cabbage	Cabbage	None
Brassica Vegetable (5A)	3/2/2016 (47567025)	Cauliflower	Cauliflower	Broccoli or Cauliflower
Cucurbit Vegetables (9)	3/2/2016 (47567030)	Cucumber	Cucumber	None
Cucurbit Vegetables (9)	3/2/2016 (47567030)	Summer Squash	Pumpkin	None
Cucurbit Vegetables (9)	3/2/2016 (47567030)	Muskmelon	Watermelon	Watermelon or Cantaloupe

Cucurbit Vegetables (9)	3/2/2016 (47567030)	Muskmelon	Cantaloupe	Watermelon or Cantaloupe
Citrus Fruit (10-10)	3/2/2016 (47567031, 49242802)	Grapefruit	Grapefruit	None
Citrus Fruit (10-10)	3/2/2016 (47567031, 49242802)	Lemon	Lemon	None
Citrus Fruit (10-10)	3/2/2016 (47567031, 49242802)	Orange	Tangerines	None
Stone Fruit (12-12)	3/2/2016 (47567033)	Plums	Apricot	None
Stone Fruit (12-12)	3/2/2016 (47567033)	Peaches	Peach	None
Stone Fruit (12-12)	3/2/2016 (47567033)	Cherries	Sweet Cherry	None
Berry and Small Fruit (13-07G)	3/2/2016 (47372605) 2/2/2012 (47372605)	Strawberry	Strawberry	None
Tree Nuts (14-12)	2/2/2012 (47567020)	Almond and Pecan	Pistachio	None

[1]All residue data submitted by registrant were conducted on representative crops listed in this column
[2]Minor use sites proposed by the registrant

MINOR USE ANALYSIS

The USDA Census of Agriculture provides the data on crops grown in the United States (USDA 2017). For all sites listed in Table 1, the total U.S. acreage for each crop is less than 300,000 acres. Acreage reported by Bayer (2018) may be different from BEAD's analysis because the registrant used USDA NASS information instead of the Census of Agriculture in some cases. See PRN 2018-1, *Pesticides: Guidance for Registrants on the Determination of Minor Use*, available at registration.gov, docket EPA-HQ-OPP-2015-0814-0016 for a detailed explanation of appropriate sources for crop acres grown. Note, that for orchard crops such as apricot, cherries, grapefruit, lemons, oranges, peaches, and pistachios, BEAD relied on bearing age acres per consultation with the United States Department of Agriculture (USDA) (USEPA, 2018). BEAD confirmed that all 16 proposed sites qualify as minor crops as each is grown on less than 300,000 acres annually.

Table 2. Acreage of crops considered for extension of exclusive use for Fluopyram

Minor Use	Claimed Acreage	Crop Acres Grown [A]	Criterion Claimed (Target Pest)
Sweet Potato	161,600	99,293	II and IV (nematodes)
Broccoli	130,500	135,185	II and IV (nematodes)
Cabbage	62,000	72,296	II and IV (nematodes)
Cauliflower	43,100	50,331	II and IV (nematodes)
Cucumber	125,800	119,655	II and IV (nematodes)
			III (powdery mildew)
Pumpkin	73,230	93,563	II and IV (nematodes)
			III (powdery mildew)
Watermelon	138,600	129,790	II and IV (nematodes)
			III (*Didymella bryoniae*)
Cantaloupe	58,000	71,436	II and IV (nematodes)
			III (powdery mildew)
Grapefruit	60,400	64,790	II and IV (nematodes)
Lemon	54,300	59,001	II and IV (nematodes)
Tangerines	66,400	56,883	II and IV (nematodes)
Apricot	9,700	12,179	II and IV (nematodes)
Peach	94,070	94,836	II and IV (nematodes)
Sweet Cherry	91,700	93,866	II and IV (nematodes)
Strawberry	52,700	137,455	II and IV (nematodes)
			III (*Botrytis cinerea*)
Pistachio	239,300	247,872	III (Alternaria alternata)

[A] USDA Census of Agriculture 2017, shown as bearing acres where applicable (perennial/orchard crops).

SUPPORT TO QUALIFY FOR CRITERIA

Requirements for Criterion II, Alternatives Pose Greater Risks to Environment or Human Health. If a pesticide was registered recently under reduced risk status, EPA presumes that the alternative pesticides pose greater risks than the active ingredient being considered for an extension of data exclusivity.

Requirements for Criterion III, Pesticide Plays a Significant Part in a Resistance Management Program. BEAD considers that Criterion III has been met in situations where there is reliable information that the chemical being evaluated is used 1) to delay the development of pest resistance to other chemicals with different Modes of Action, or 2) where one or more of the target pests have already developed resistance in the U.S. to alternative chemicals.

Requirements for Criterion IV, pesticide plays or will play a significant part in an Integrated Pest Management Program. BEAD considers Criterion IV has been met in situations where there was information that the chemical being evaluated is useful in managing target pests with low-to-no impact on other aspects of integrated pest management or IPM such as inclusion of non-chemical pest control tactics.

ASSESSMENT OF CRITERIA

Applicability of Criterion II to fluopyram

The registrant claims fluopyram qualifies under criterion II for 15 of their 16 proposed minor used sites, excluding only pistachios. However, BEAD's Extension of Exclusive Use assessments are limited to the benefits an active ingredient offers the grower and will not make the determination of criterion II as it is a risk-based determination. Therefore, BEAD defers to the Registration Division to determine if registered alternatives to fluopyram pose greater risks to the environment or human health.

Applicability of Criterion III to fluopyram

The registrant claims that fluopyram will play an important role in resistance management for the following crops and pests: cucumber, cantaloupe, pumpkin, pistachio, strawberry and watermelon for the control of various fungal pathogens such as *Botrytis, Alternaria, Didymella*, and powdery mildews. While fluopyram is one of several succinate dehydrogenase inhibitors or SDHI's fungicides available to growers it has been shown to exhibit efficacy on SDHI-resistant mutant populations that are no longer controlled by other SDHI active ingredients (Amiri et al., 2014; Avenot et al., 2011 and 2014; Fairchild et al., 2013; Mallik et al., 2013; see Bayer 2018). The registrant also provided evidence of how fluopyram fits into a fungicide rotation that will help alleviate selection pressure on other classes of fungicides such as the quinone outside inhibitors or QoI and the Demethylation Inhibitors or DMI type fungicides, of FRAC group 11 and 3 respectively, prolonging their efficacy and staving off the development of resistance within the target fungal population (Mcgrath 2015; see Bayer 2018).

Bayer (2018) identified extension materials explaining how growers can utilize fluopyram in the management of resistant fungal populations in several crops (Keinath, 2018; UC Tree Crop Guide, 2017). According to MRD between 2013-2017, fluopyram was the top fungicide by total acres treated targeting *Alternaria spp*. in pistachio crops surveyed. Therefore, BEAD concludes

that fluopyram satisfies criterion III and will play an important role in the resistance management of key pathogens in pistachio, strawberry and the cucurbit crops listed above. This results from representative crop residue data only being allowed to represent minor uses on a 1-for-1 basis. The registrant provided data on 3 representative crops for the cucurbit crop group, therefore only 3 of the 4 cucurbit minor uses proposed (cucumber, pumpkin, and watermelon or cantaloupe) by the registrant are supported by data and would count toward the nine required sites (See Table 1). Pistachio, strawberry and three of the four cucurbit crops identified (cucumber, cantaloupe or watermelon, and pumpkin) qualify under criterion III.

Applicability of Criterion IV to fluopyram

The registrant claims that fluopyram plays or will play a significant role in integrated pest management plans based on its use as a nematicide within the several of the proposed minor crops (See Table 2). As the cucurbit crops in addition to strawberry and pistachios have already qualified for criterion III, these uses will not be considered for criterion IV as to not be double counted. Since only four additional crops must qualify to meet the nine required sites to achieve the full three years of data exclusivity BEAD focused on sweet potato, the three brassicaceous crops (broccoli, cabbage, and cauliflower), and sweet cherry for the analysis of criterion IV. BEAD verified that fluopyram is the only SDHI fungicide registered for control of plant pathogenic nematodes although its current mode of action as nematicide is unknown (Heiken, 2017).

In sweet potato, according to the North Carolina State Extension, a major sweet potato producing state, products such as Velum Prime (fluopyram) provide growers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne spp.),* even providing better control than some older chemistries such as oxamyl (Quesada-Ocampo, 2018; See Bayer, 2019). Nematicides such as fluopyram offer increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives.

For crops within the brassica crop group, including broccoli, cabbage and cauliflower, the University of California agriculture extension states that fluopyram products, such as Velum One and Velum Prime, offer growers another tool to combat the impacts of pest such as root knot nematodes in several vegetable crops (Nunez, 2017; See Bayer, 2019). The registrant provided efficacy data showing fluopyram as a top performer in the reduction of nematodes populations within the crop root zone (Desaeger, 2018). They also provided discussion on how these newer nematicide products are selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increased flexibility in using them and opportunities for increased soil nutrient management and integrated pest management techniques to be practiced (Nunez, 2017; Desaeger, 2018; See Bayer, 2019).

In orchard crops such as sweet cherry fluopyram offers growers a more selective tool to combat nematode issues that arise after orchard establishment. Fluopyram offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong

IPM programs and more sustainable stewardship practices (UC Tree Crop Guide, 2017; Quintanilla, 2019; See Bayer, 2019)

BEAD concludes that fluopyram does offer growers enhanced opportunity to practice IPM relative to the identified nematicide alternatives. The registrant's amended package (Bayer, 2019) provides crop specific information that speaks to how fluopyram will play an important role in an IPM programs to satisfy criterion IV. For example, use of more selective nematicides provides growers the opportunity to practice greater soil nutrient and microbial management than with sterilization that results from fumigant applications (Heiken, 2017; Quesada-Ocampo,2018; Nunez, 2017; Desaeger, 2018; See Bayer, 2019). Therefore, based on the available information provided in the original package and amended submission (Bayer 2018 and Bayer, 2019), BEAD finds sweet potato, broccoli or cauliflower, cabbage, and sweet cherry to meet criterion IV for extension of data exclusivity.

CONCLUSION

BEAD finds the registrant provided sufficient evidence to support extension of exclusive use of data under FIFRA Section 3(c)(1)(F)(ii) for at least nine minor use sites required to attain three additional years of data exclusivity under criterion III and IV. BEAD found that for crops such as cucumber, pumpkin, watermelon, canataloupe, strawberry and pistachios, fluopyram provides growers with a new tool to manage resistant fungal disease satisfying criterion III. BEAD also concluded that fluopyram will play an important role in an integrated pest management program within the following crops: broccoli, cabbage, cauliflower, sweet potato and sweet cherries thus satisfying criterion IV.

REFERENCES

Amiri, 2014. "*Resistance to Fluopyram, Fluxapyroxad, and Penthiopyrad in Botrytis cinerea from Strawberry*." Plant Diseases. 98:532-539. 2014. See Bayer, 2018

Avenot et al., 2011. "*Molecular characterization of boscalid- and penthiopyrad-resistant isolates of Didymella bryoniae and assessment of their sensitivity to fluopyram."* Pest Management Science, doi: 10.1002/ps.2311. Epub 2011 Nov 10. See Bayer, 2018

Avenot et al., 2014. "*Sensitivities of Baseline Isolates and Boscalid-Resistant Mutants of Alternaria alternata from Pistachio to Fluopyram, Penthiopyrad, and Fluxapyroxad.*" Plant Diseases 98:197-205. See Bayer, 2018

Bayer Crop Sciences. 2018. Fluopyram Minor Use Registrations Petition for 3 Years Extension of Exclusive Use Data Protection Provided under FIFRA Section 3(c) (1) (F) (ii). (MRID 50642501)

Bayer Crop Sciences. 2019. Amended Fluopyram Minor Use Registrations Petition for 3 Years Extension of Exclusive Use Data Protection Provided under FIFRA Section 3(c) (1) (F) (ii). (MRID 50872501)

Desaeger, 2018. "*New Nematode Management Options for Vegetables and Strawberries*" University of Florida. June 31, 2018. See Bayer, 2019

Fairchild et al. 2013. "*Assessing fungicide resistance in populations of Alternaria in Idaho potato fields.*" Crop Protection 49, 31-39. March 11th, 2013. See Bayer, 2018

Fungicide Resistance Action Committee (FRAC). 2019. FRAC Code List. http://www.frac.info/docs/default-source/publications/frac-code-list/frac-code-list-2019.pdf?sfvrsn=98ff4b9a_2 [Accessed April 2019]

Heiken, 2017. The Effects of Fluopyram on Nematodes. 2017. Department of Plant Pathology. North Carolina State [Accessed May 2019] See Bayer, 2018 Universityhttps://repository.lib.ncsu.edu/bitstream/handle/1840.20/33746/etd.pdf?sequence=1

Keinath, 2018. "Managing Foliar Diseases on Watermelon and Other Cucurbits with Fungicides." Clemson University, Presented at: 2018 Great Plains Growers Conference. See Bayer, 2018

Market Research Data (MRD). 2013-2017. Data collected and sold by a private market research firm. Data collected on pesticide use for about 60 crops by annual surveys of agricultural users in the continental United States. Survey methodology provides statistically valid results, typically at the state level.

Mallik et al., 2013. "*Molecular Characterization and Detection of Mutations Associated with Resistance to Succinate Dehydrogenase-Inhibiting Fungicides in Alternaria solani.*" Disease Control and Pest Management. Phytopathology 104:40-49. 2014. See Bayer, 2018

McGrath, 2015. "*Cucurbit Powdery Mildew in the USA."* Plant Pathology & Plant-Microbe Biology Section, Cornell University. 2015. See Bayer, 2018

Nunez, 2017. "*Update on Evaluation of New Nematicides.*" University of California; Kern County Vegetable Crop Extension. December, 2017. See Bayer, 2019

Quesada-Ocampo, 2018. "*Sweet Potato Root Knot Nematode: Vegetable Pathology Fact Sheet*" NC State Extension. May 24, 2018. See Bayer, 2019

Quintanilla, 2019. "*New options available for battling orchard nematodes."* Fruit Growers Network. February 4th, 2019.

USDA. 2017. Census of Agriculture. National Agricultural Statistics Services (NASS). United States Department of Agriculture (USDA). Released April, 2019. Available at https://agcensus.usda.gov/Publications/2017/ [Accessed April 2019]

USEPA. 2018. Pesticide Registration (PR) Notice 2018-1: Pesticides: Guidance for Registrants on the Determination of Minor Use. Available at: https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year