




OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION


WASHINGTON, D.C. 20460

April 17, 2024

MEMORANDUM

SUBJECT: Review of a Petition by BASF for the Extension of Exclusive Use of Data for Cyflumetofen (PC# 138831)

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Product Review Panel Date: February 14, 2024

SUMMARY

BASF petitioned the Environmental Protection Agency (EPA), under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Section 3(c)(1)(F)(ii), to extend the exclusive use period for data supporting the registration of cyflumetofen, a miticide, for three years. For extension of exclusive use of data, use of the pesticide on a minor crop needs to meet one of the four criteria. BASF claims cyflumetofen plays an important role in miticide resistance management and in integrated pest management programs, thus satisfying Criterion III and Criterion IV, respectively, for extending the exclusive use period of cyflumetofen as defined under FIFRA 3(c)(1)(F)(ii) in all claimed crops. BASF cited the following minor use crops (less than 300,000

acres) as qualifying for these two criteria: certain greenhouse-grown fruiting vegetables (tomatoes, bell pepper, non-bell pepper, and eggplant crops); greenhouse-grown strawberries; greenhouse-grown cucumbers; certain field grown stone fruits (peach, sweet and tart cherries, plum, plumcot, nectarines, prunes, and apricot) and hops. This amounts to a total of 15 crops.

A request for extension of exclusive use may be made at any time prior to the expiration of the initial exclusive use period. In 2018, BEAD reviewed a previous request for extension of exclusive use for cyflumetofen and concluded that eight crops met at least one of the required criteria and qualified as minor crops under FIFRA's acreage-based definition. These crops were lemons, grapefruits, pears, and strawberries, and minor crop members of the citrus, tree nut and pome fruit crop groups (e.g., tangerines, macadamia nuts, hazelnuts, and Asian pears). Based on that determination, EPA extended the exclusive use period for cyflumetofen by two years based on six of the eight crops. Therefore, two crops (that were determined to meet at least one of the required criteria and qualified as minor crops) are available to support an additional year of extension. Only one additional qualifying minor crop is needed. Therefore, this analysis does not need to assess all 15 use sites in the current submission.

BEAD finds that at least two crops included in the registrant's current request qualify as minor uses: peaches and plums. BEAD concludes that cyflumetofen meets the extension of exclusive use Criteria III and IV for both peaches and plums, which qualify as minor crops under the FIFRA definition. Therefore, peaches and plums bring the total number of crops qualifying for an extension of exclusive use (EEU) to 10, given that eight other crops were found to qualify in BEAD's 2018 review. An applicant needs nine qualifying crops to get the maximum number of three years of additional data protection.

REGULATORY 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 three additional years, if registered within seven years of the commencement of the exclusive use period and the registrant demonstrates that one or more of the following conditions are met for crops that have supporting residue data provided as part of the registration:

- (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 pesticide plays or will play a significant part in an integrated pest management program.

A minor use is defined in FIFRA Section 2(II) 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 subgroup is equal to the number of representative crops for which residue data have been submitted. 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.

REQUIREMENTS TO QUALIFY FOR THE CLAIMED CRITERIA

Requirements for Criterion I, there are insufficient efficacious alternative registered pesticides for the use site. EPA considers Criterion I to be met in situations where the pesticide: 1) fills a void in the current pest control program (e.g., unique timing window); 2) controls a broader spectrum of pests than currently registered alternatives; 3) controls a different life stage for the pest; or 4) provides a crucial timing advantage (e.g., shorter pre-harvest interval or re-entry interval).

Requirements for Criterion II, the alternatives to the minor use pesticide pose greater risks to the environment or human health. BEAD cannot evaluate risks and does not provide the registration division with information related to Criterion II.

Requirements for Criterion III, the minor use pesticide plays or will play a significant part in managing pest resistance. EPA considers Criterion III to be met in situations where there is reliable information that the chemical being evaluated is used either to delay the development of pest resistance to other chemicals with different modes of action or where one or more of the target pests have already developed resistance in the U.S. to alternative chemicals.

Requirements for Criterion IV, the minor use pesticide plays or will play a significant part in an integrated pest management program. EPA considers Criterion IV to be met in situations where there is reliable information that the chemical being evaluated is useful in managing target pests while having low-to-no impact on other aspects of integrated pest management (IPM), such as inclusion of non-chemical pest control strategies (primarily biological control using insect natural enemies).

OVERVIEW OF THE REGISTRANT SUBMISSION

Cyflumetofen, a member of the beta-ketonitrile derivatives class of chemistry, is a miticide first registered in 2014. Cyflumetofen’s mode of action is to disrupt respiration, because it is a

mitochondria complex II electron transport inhibitor. It is categorized in Group 25A, according to the Insecticide Resistance Action Committee (IRAC 2023). It is currently the only Group 25A active ingredient (AI) that is registered for use in the United States. Labeled target pests are all web spinning spider mites (Family Tetranychidae). It is a contact miticide for use against all life stages (eggs, nymphs, and adults).

In 2017, BASF submitted to EPA a request for extension of exclusive use. In 2018, EPA granted two of the three allowed years of extension through May 9, 2026. Because only eight crops/crop groups were supported by residue data, BASF did not qualify for a three-year extension. With the current submission, BASF requested EPA review new supporting data on several other minor crops, thus requesting BASF's exclusive use period a third year (through May 9, 2027). The registrant stated that cyflumetofen satisfies two of the FIFRA Section 3(c)(1)(F)(ii) requirements for the following use sites: certain greenhouse-grown fruiting vegetables (tomatoes, bell pepper, non-bell pepper, and eggplant crops); greenhouse-grown strawberries; greenhouse-grown cucumbers, certain field grown stone fruits (peach, sweet and tart cherries, plum, plumcot, nectarines, prunes, and apricot), and hops (a total of 15 crops). The registrant claimed that cyflumetofen plays a part in miticide resistance management, and/or an integrated pest management program (relevant to criteria III and IV, respectively) for each of the claimed minor use sites and provided supporting information.

SUPPORT TO QUALIFY FOR THE CRITERIA EVALUATED BY BEAD

Requirements for Criterion III, the minor use pesticide plays or will play a significant part in managing pest resistance.

To support criterion III, the registrant stated that cyflumetofen is the only member of its IRAC MOA group that is currently registered in all listed crops in the US. They also stated that many of the mites it can control are prone to developing resistance to multiple MOAs frequently; they stated that this is particularly true of spider mites, which can damage all of the crops that cyflumetofen is registered for. The registrant submission also pointed out that alternating (also called "rotating") miticide active ingredient MOAs across multiple treatments is a key basic component of reliable resistance management programs and asserted that cyflumetofen provides value as a member of effective resistance management programs aimed at mite pests in all crops, mainly because of its unique MOA.

Requirements for Criterion IV, the minor use pesticide plays or will play a significant part in an integrated pest management program.

To support criterion IV, the registrant summarized information from Koppert, a company that provides mass-reared biological control agents (insect and mite predators and parasitoids) for a wide range of pests, including the spider mites that cyflumetofen can target (Koppert, 2023). In addition to providing supplies to growers and other interested parties of biological control organisms, Koppert also maintains a publicly available database of the level of mortality that several insecticides and miticides have on beneficial natural enemies such as predatory and parasitic insects and mites that should be part of IPM programs (Koppert, 2023). The registrant

provided tables summarizing Koppert's characterization of cyflumetofen's impacts on several predatory mites that can be used or fostered in fields to suppress phytophagous mites such as the spider mite. Koppert (2023) described cyflumetofen in comparison to several commonly available miticide alternatives such as abamectin, propargite, and etoxazole. The information summarized indicated that cyflumetofen causes low mortality to predatory mites when compared to such alternatives. The registrant also pointed out that cyflumetofen is highly selective for mites and so should be expected not to cause significant mortality of non-target beneficial arthropods (predatory and parasitic insects, predatory mites, spiders) that typically occur in agricultural habitats.

The registrant also pointed to IR-4's Pesticide Clearance Requests, documents used to describe pesticides that are to be supported by IR-4 for registration in a minor crop. They stated that in this document, agricultural stakeholders indicated that cyflumetofen was requested for registration based on its suitability for use in IPM programs for mite control and that it offers a MOA different from existing products to manage resistance to miticides.

BEAD ANALYSIS

BEAD first confirms that residue trial data are sufficient such that there is a one-for-one relationship for each use site. Then, BEAD confirms that each crop meets the definition of a minor crop per FIFRA Section 2(II)(1), wherein each crop must be grown on less than 300,000 acres in the U.S. by consulting the most recent Census of Agriculture conducted by the United States Department of Agriculture (USDA) National Agricultural Statistics Service (NASS). Finally, BEAD evaluates the evidence submitted by the registrant to determine if the claimed criteria are met. If BEAD finds nine qualifying use sites meet at least one claimed criterion, the evaluation is complete, as that is the requirement for the maximum three-year extension of data exclusivity.

In 2018, BEAD found that eight minor use sites satisfied at least one criterion for extension of exclusive use. The eight crops and crop groups were lemons, grapefruits, pears, and strawberries, and minor crop members of the citrus, tree nut and pome fruit crop groups (e.g., tangerines, macadamia nuts, hazelnuts, and Asian pear) (Mallampalli 2018). At that time, EPA extended the exclusive use period for cyflumetofen by two years based on six of the eight crops. The following analysis is a review of a subset of the 15 additional use sites to determine if a ninth site qualifies to extend the exclusive use period one additional year.

Residue Trials

BEAD confirmed with the Registration Division that the uses listed in the registrant's current submission are supported by residue data.

Minor use Analysis

BEAD excluded hops from consideration because this use was not registered within seven years of the commencement of the exclusive use period; hops registration was in December 2021. Of the other 14 crops and commodities listed by the registrant in the current submission, BEAD confirmed that at least two field grown crops, peaches and plums, qualify as minor uses (<300,000 acres) since their national acreages are approximately 113,000 and 17,000 acres respectively, based

on the most recent Census of Agriculture (USDA, 2017).

Because peaches and plums clearly qualify as minor uses, and only one additional crop is needed to grant the registrant's request, BEAD did not review acreage requirements of the other submitted use sites.

Applicability of EEU criteria

BEAD reviewed extension literature and the suite of available miticides for peaches and plums to confirm whether or not at least one of the two EEU criteria claimed by BASF were reasonably applicable. BEAD did not further evaluate the other submitted crops.

Criterion III focuses on the resistance management utility of the AI in question. BEAD confirmed that cyflumetofen continues to be the only member of its biochemical mode of action (IRAC Group 25A) that is registered in the US at this time. In addition, BEAD found research and extension literature indicating that spider mites (e.g., twospotted spider mite, *Tetranychus urticae*), the main pest for which cyflumetofen is a recommended miticide (Muehlbauer et al. 2023, Beckerman et al. 2022, LSU, 2023, Studebaker, 2023), are well known for their propensity to develop resistance to many miticide modes of action (Xu et al. 2018). Depending on the region, spider mite populations have developed at least isolated resistance to at least 10 miticide modes of action, out of a total of 16 currently registered in the US (IRAC 2019). Resistance can manifest rapidly, particularly with twospotted spider mite, and is likely due to a combination of factors, including the wide host plant range of these mites (which increases population exposure to repeated applications of the same miticides in many crop systems, and thus increasing selective pressure in favor of resistance). Other important factors are a high reproductive rate and rapid life cycle (Xu et al. 2018). Spider mites have a very wide host plant range and are known to attack and potentially cause serious damage in all of the crops listed in the registrant's request, including peaches and plums (Beckerman et al. 2023, Muehlberger et al. 2023).

Based on these findings, BEAD concludes that for all crops listed in the request, cyflumetofen does serve as part of a pest management strategy to delay the development of pest resistance to other miticides with different modes of action and is likely used in situations where one major target pest, spider mites, have already developed resistance in the U.S. to alternative miticides. Therefore, for adequate control of these pests, growers often need multiple applications of miticides throughout the year with as many different modes of action as possible. Therefore, Criterion III is applicable to this request for peaches and plums.

The registrant also asserted that Criterion IV (role of the AI in IPM) applies to cyflumetofen because it has low-to-no impact on non-chemical pest control strategies (such as biological control, cultural practices such as growing plants in nearby habitat that attract pests away from a crop or attract natural enemies of pests towards a crop field) that are part of an IPM program. In its own registration review work, BEAD has used the Koppert side-effects database that the registrant cited as support for Criterion IV and considers it a reasonably valid source of such information. However, the Koppert database is somewhat limited in that it only provides a qualitative description of the data underlying its descriptions of negative effects of pesticides on biological control agents such as predatory and parasitic arthropods.

To take this limitation into consideration, BEAD reviewed scientific literature published on the effects of cyflumetofen on natural enemies of spider mites (as well as several other crop damaging mites). Results from a recent study (Bergeron and Schmidt-Jeffris, 2020) show low to moderate lethal impacts of cyflumetofen on three predatory mites commonly used to control spider mites: *Phytoseiulus persimilis*, *Neoseiulus californicus*, and *N. fallacis*. Several other studies mentioned by Bergeron and Schmidt-Jeffris have also found low negative effects of cyflumetofen on other predatory mite species. Bergeron and Schmidt (2020) go so far as to clearly state that these studies, along with their own results, indicate that “the available literature on cyflumetofen suggests that cyflumetofen is appropriate for use in IPM”. It is important to keep in mind that spider mites can reach damaging levels multiple times during a growing season, so multiple miticide treatments are necessary in affected crops, especially in prolonged hot, dry conditions, which foster spider mite population growth (Ximenez-Embun et al. 2017, Cullen 2012). Thus, even in situations where other IPM-compatible miticides are available, cyflumetofen offers IPM-related value to growers who want to use miticides more sustainably.

Based on the review above, BEAD concludes that Criterion IV also applies to the EEU request for cyflumetofen use in peaches and plums.

CONCLUSION

BEAD finds that at least two crops included in the registrant’s current request qualify as minor uses: peaches and plums. In addition, for these crops BEAD concludes that cyflumetofen clearly qualifies for Criterion III and Criterion IV also. Peaches and plums bring the total number of crops qualifying for an EEU extension to 10, given that eight other crops were found to qualify in BEAD’s 2018 review.

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