Proposed Registration of Sulfoxaflor for Use on Agricultural Crops, Ornamentals and Turf

Approved by: _____

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Proposed Registration Decision for Sulfoxaflor

Proposed Regulatory Decision

The Environmental Protection Agency (EPA) is proposing to unconditionally grant, under section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), registrations for the active ingredient sulfoxaflor, formulated as a technical product and two end-use products. The proposed formulation for manufacturing, "Sulfoxaflor Technical," contains 97.9% sulfoxaflor (EPA Reg. No. 62719-631). Transform® WG, (EPA Reg. No. 62719-625) is a water-dispersible granule formulation and contains 50% sulfoxaflor. An aqueous suspension concentrate, "Closer® SC" containing 21.8% sulfoxaflor is also proposed (EPA. Reg. No. 62719-623).

Background

On August 19, 2010, EPA received the application for registration of sulfoxaflor, a new active ingredient, submitted by Dow AgroSciences (DAS). In collaboration with counterpart agencies in Canada and Australia, EPA conducted a "Global Joint Review" (GJR) of sulfoxaflor. In order for a compound to be considered eligible for evaluation as an international project initiated as a GJR, all the data requirements of all participating regulatory authorities must be addressed. The sulfoxaflor dossier was determined to contain all the data required by the Australian Pesticides and Veterinary Medicine Authority, the Canadian Pest Management Regulatory Authority and the U.S. EPA. Scientists from the three authorities reviewed the full dossier, peer reviewed the primary evaluations conducted by their international colleagues, and communicated extensively on specific disciplines and issues. Upon completion of the GJR and after public comment, EPA granted an unconditional registration of sulfoxaflor on May 6, 2013.

On July 2, 2013, the Pollinator Stewardship Council and others, petitioned for review of the sulfoxaflor registration in the Ninth Circuit Court of Appeals. On September 10, 2015, the Court issued its opinion, finding that the registration was not supported by substantial evidence to demonstrate no unreasonable adverse effects to honey bees resulting from the registration of sulfoxaflor. Although the initial sulfoxaflor submission contained all the data required by EPA regulations for registration of a new agricultural insecticide, the Court vacated the registrations and remanded them to EPA to "obtain further studies and data regarding the effects of sulfoxaflor on bees as required by EPA regulations." The vacatur of the sulfoxaflor registrations became effective November 12, 2015. As the registrations were no longer in effect under FIFRA, on the same date EPA issued a cancellation order to address existing stocks. Although the product registrations were vacated, the tolerances for sulfoxaflor residues on treated commodities that were established under the Federal Food, Drug and Cosmetic Act, remain in place.

Following the remand, EPA has re-evaluated the sulfoxaflor application that was amended by DAS to further reduce/eliminate exposure to pollinators by restricting applications to post-bloom only for all proposed crops that are attractive to bees. Additionally, indeterminate blooming

crops that had been registered (citrus, cotton, cucurbits, soybeans and strawberry) are not included in this proposed registration.

The crops proposed for registration, designated by their attractiveness to bees, are:

Not Bee Attractive:

- Barley, triticale, wheat
- Turf grass

Harvested Before Bloom:

- Brassica leafy vegetables
- Bulb vegetables
- Leafy vegetables (non-Brassica) and watercress
- Leaves of root and tuber vegetables
- Root and tuber vegetables

Bee Attractive but Applications Post-Bloom Only:

- Berries (Grape, Blueberry, Cranberry)
- Canola
- Fruiting Vegetables (Tomato, Pepper, Eggplant) and Okra
- Pome fruit
- Ornamentals
- Potato
- Stone Fruit
- Succulent and Dry Beans
- Tree nuts and pistachio

Limiting the use of sulfoxaflor to the above listed crops, and restricting the timing of applications results in essentially no exposure to bees on the treated field.

Evaluation

Potential Risks

The toxicological effects and end points used in the human health risk assessment[1] are unchanged from the original evaluation and no additional data were required. All of the risk estimates are well below EPA's level of concern (LOC). The aggregate dietary risk assessment (food + drinking water exposure) without any refinement to adjust for over-estimation of risk resulted in an acute dietary risk estimate range from 4% to 16% of the acute population-adjusted dose (aPAD), with the highest risk estimates being for children 1-2 years old and females 13-49 years old. The chronic dietary risk estimates range from 5% to 18% of the chronic population-adjusted dose (cPAD) with the highest risk estimate estimated for infants. Handler exposure and

[1] Sulfoxaflor: New Active Ingredient Human Health Risk Assessment of Uses on Numerous Crops; Sept. 26, 2012

occupational post-application exposure are also not of concern.[2] The conclusions from the human health risk assessment were based on a broader set of uses than what is currently proposed for registration since the five indeterminate-blooming crops are not included. The risk assessment was not redone since no risks were identified.

The ecological characterization of sulfoxaflor integrates conservative exposure and toxicity estimates to generate a risk quotient (RQ) for non-target organisms.[3] Because the risks to non-target organisms were found to be low in the previous ecological risk assessment, EPA has not conducted another comprehensive assessment based on the application restrictions in DAS's amended application. The RQs are compared to the LOCs to evaluate the potential of adverse ecological effects. An RQ is not a bright line that is clearly defined and interpreted; rather, it provides an indication of potential risk that may need to be mitigated. If potential risk remains after mitigation measures are applied, EPA evaluates those remaining risks against the benefits provided by the pesticide.

The ecological assessment concluded that sulfoxaflor poses a low potential for acute risk to listed (endangered) and non-listed fresh and saltwater fish (acute RQs <0.01 for both compared to listed and non-listed LOCs of 0.05 and 0.5, respectively). The maximum chronic RQ was 0.08 for freshwater fish and 0.04 for saltwater fish, both are below the LOC of 1. The acute risk to freshwater and saltwater invertebrates is below the listed and non-listed LOCs (RQs <0.01 for both). The chronic risk LOC is not exceeded for either fresh or saltwater invertebrates (maximum RQ of 0.5). No risks were identified for vascular and non-vascular aquatic plants.

The LOCs for terrestrial vertebrate animals are 0.1 for acute risk to listed species, 0.5 for acute risk to non-listed species and 1 for chronic risk (listed and non-listed species). The acute risk to mammals is below the listed and non-listed LOCs (maximum RQ of 0.02), while the chronic risk slightly exceeds the LOC with a maximum RQ of 3.8. There is low potential for acute and chronic risk to birds based on the maximum acute RQ of 0.01 and a maximum chronic RQ of 0.3. Risks to terrestrial plants were also not indicated in the ecological risk assessment.

In the proposed label for sulfoxaflor, no exposure (and no risk) is expected on the treated field to bees because, for crops that are bee-attractive and not harvested before bloom, all applications will be restricted only to periods post-bloom for bee-attractive crops. For crops that are harvested prior to bloom (ex. lettuce, onions), the label will prohibit application to these crops that are grown for seed production.

All foliar spray applications (regardless of pesticide) are subject to potential drift to areas adjacent to the treated field where bees may be present. With sulfoxaflor, the following label restrictions have been required to minimize spray drift and potential exposure of bees foraging on plants adjacent to treated fields:

- Applications are prohibited above wind speeds of 10 mph

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[2] Sulfoxaflor. Occupational and Residential Exposure and Risk Assessment to Support the Registration of the New Active Ingredient on a Variety of Food Crops, Turfgrass (Sod Farms) and Ornamentals; Sept. 18, 2012

[3] Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration; November 19, 2012

- Applications must be made with medium to coarse spray nozzles

Given there is essentially no exposure to bees on the field and the restrictions imposed to minimize spray drift will reduce exposure to bees off the field, EPA does not think a screening-level risk assessment would have been necessary to make a finding of no unreasonable adverse effects. Nevertheless, EPA has a significant amount of data on sulfoxaflor's effects to bees so the Agency conducted a spray drift analysis to better characterize the potential risks off the field. A spray drift analysis indicates that the spatial extent of acute risks beyond the treated field is very limited (<1 – 12 feet beyond the treated field). Therefore, a spray drift buffer of 12 feet would be expected to eliminate acute risk to bees that may be foraging in this zone adjacent to treated fields. For chronic risks to individual bees, a bounding analysis suggests that estimated chronic risks are also spatially limited beyond the treated field (2-49 feet, depending on modeling and toxicity assumptions). In addition to being spatially limited, available data suggest that the temporal extent of acute and chronic risks beyond the treated field is also limited to relatively short periods of time (*e.g.*, half of sulfoxaflor degrades in pollen and nectar within 9 days or less based on the vast majority of data). The acute and chronic drift analyses rely on several assumptions that collectively are to likely overestimate off-site exposure (and risk) to bees. These include assuming that: 1) plants in the spray drift zone are blooming at the time of application, 2) 100% of the bee's diet comes from the blooming plants inhabiting the spray drift zone, and 3) residues in pollen and nectar of plants in the spray drift zone equate to the maximum residues observed in submitted studies. From a colony perspective, honey bees are known to forage over long distances from the hive (up to 5 miles) and from a wide variety of floral resources. Given these assumptions, off-site risks to bees appear limited both spatially and temporally.

Benefits

Sulfoxaflor has a novel mode of action that is distinct from all registered alternative insecticides. According to the Insecticide Resistance Action Committee, sulfoxaflor is a sulfoximine and the only member of a new subclass (Group 4C) that targets the nicotinic acetylcholine receptor in insects. The structure of sulfoxaflor makes it stable in the presence of a monooxygenase enzyme that was shown to degrade a variety of neonicotinoids (Group 4A). The stability results in a broad lack of cross-resistance to neonicotinoids and other insecticide families. Although the target receptor is the same site as Group 4A chemicals such as acetamiprid and imidacloprid, the mode of action is different and unique to sulfoxaflor. As a result, sulfoxaflor will work on target pests that insecticides in Groups 1A and 1B (carbamates and organophosphates), Group 3A (pyrethroids) and the Group 4A neonicotinoids, fail to control, unless used as tank mixes and/or with multiple applications.

The ecological risk profile of sulfoxaflor is very favorable compared to its alternatives. Organophosphates such as chlorpyrifos, acephate and dimethoate are toxic to fish, aquatic invertebrates, small mammals, wildlife and/or birds. Carbamates are also very toxic to non-target organisms. For example, the label for carbaryl, a carbamate, states: "this product is extremely toxic to aquatic invertebrates" and another carbamate, oxamyl, is labeled with "This

pesticide is toxic to aquatic organisms (fish & invertebrates) and extremely toxic to birds and mammals."

Pyrethroids such as lambda-cyhalothrin and bifenthrin are extremely toxic to fish and aquatic invertebrates." Clothianidin, a neonicotinoid, is toxic to aquatic invertebrates and thiamethoxam, also a neonicotinoid, is toxic to wildlife and highly toxic to aquatic invertebrates. Sulfoxaflor, however, is not toxic to fish or aquatic invertebrates, and has low potential for risk to mammals or birds. Since there is no hazard to these non-target organisms, there is no requirement for toxicity statements regarding fish, aquatic invertebrates, mammals or birds on sulfoxaflor products.

Although not available for most formulations, including the chemical classes listed above, DAS provided "RT_{25}" data on both of the sulfoxaflor end-use products, Transform and Closer. The RT_{25} refers to the residual time to 25% mortality that is derived from a study of honey bee toxicity of residues on foliage and reflects acute toxicity to bees via direct contact with treated foliage.[4] This information provides farmers and beekeepers with a means of gauging the lengths of time that specific pesticide products may remain toxic to bees and other pollinators following application of these products to plants. For the proposed sulfoxaflor products, EPA determined that an RT_{25} value could not be calculated for either the Transform or Closer formulations because the toxicity was too low, indicating that the toxicity of these formulations is short-lived in the field.

Sulfoxaflor specifically targets piercing/sucking insects such as aphids, mealybugs, psyllids, plant bugs and whiteflies. These insects are often vectors of viral and bacterial diseases, infections of which can result in complete crop loss. EPA has heard from many growers that believe sulfoxaflor is an important tool for control of resistant pests, as well as invasive species. Growers of cole crops, leafy vegetables and fruiting vegetables want to use sulfoxaflor against whiteflies, which produce honeydew that causes difficulty in harvest and reduces the quality of the produce. Whiteflies also transmit plant viruses which can seriously affect yield and quality of the crop.[5] Apple growers in Washington are concerned about the woolly apple aphid which causes chronic debilitation of the tree, with fruit contamination that results in rejection or fumigation of apples grown for export.[6] Sulfoxaflor controls woolly apple aphid while neonicotinoids show weak performance. Other crops for which growers requested the registration of sulfoxaflor for specific target pests include potatoes (psyllid), canola (aphids), and grapes (vine mealybug).[7] Pecan growers have communicated to EPA that imidacloprid is no longer effective on black margined pecan aphid and black pecan aphid. These aphid species reduce pecan quality and yield.[8] Sulfoxaflor controls these aphid species.

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[4] https://www.epa.gov/pollinator-protection/residual-time-25-bee-mortality-rt25-data

[5] EPA-HQ-OPP-2010-0889, comment 362

[6] EPA-HQ-OPP-2010-0889, comment 266

[7] EPA-HQ-OPP-2010-0889; comment 275, 279, 305, 312, 345

[8] EPA-HQ-OPP-2010-0889, comment 265

Nearly all of the crops that sulfoxaflor is proposed for use on are minor crops. These include the bulb vegetable crop group (ex. garlic, leeks, shallots), the fruiting vegetable crop group (ex. eggplant, pimento, tomatillo), the root and tuber crop group (ex. daikon, ginseng, horseradish), the small vine and low growing berry crop group (ex. gooseberry, maypop, lingonberry) and the succulent, edible podded and dry bean crop group (ex. chickpea, cowpea, wax bean), as well as crops not included in crop groupings, for example, okra, pistachio and watercress. EPA presumes that it is in the public interest to register sulfoxaflor for these minor uses.

For the proposed non-minor uses; potatoes, non-residential turfgrass and wheat, EPA considered whether registering sulfoxaflor is in the public interest because it is less risky comparatively to currently registered pesticides or whether the benefits provided by sulfoxaflor exceed those of registered alternatives or non-pesticide methods. For greenbug infestations of turfgrass, chlorpyrifos and another organophosphate, acephate, have been recommended treatments.[9] [10] The registered insecticides for aphid infestations of wheat, notably the Russian Wheat Aphid are pyrethroids such as cyfluthrin, zeta-cypermethrin and lambda-cyhalothrin.[11] Pyrethroids, are known to have a harsh effect on aquatic invertebrates and are labeled as extremely toxic. As mentioned, sulfoxaflor will be helpful to potato farmers against potato psyllid which vectors zebra chip disease.

Sulfoxaflor fits well as a critical tool in Integrated Pest Management programs, replacing multiple applications of compounds with a higher risk to humans and/or non-target organisms. Due to its unique chemistry and lack of cross-resistance to the neonicotinoid and other classes of insecticides, sulfoxaflor can be a valuable tool in managing pesticide resistance. Its' labeling displays the Mode of Action identifier and best management practice statements designed to help mitigate pest resistance that is consistent with EPA's Pesticide Registration Notice on pest resistance management.[12] Furthermore, researchers and crop consultants have commented that not only is sulfoxaflor efficacious against difficult target pests but it does not "flare" spider mites as some organophosphates like acephate does, nor does it flare aphids as pyrethroids are known to do. Researchers have observed that it is has low impact on lady beetle larvae and other beneficial insects.[13] Protecting biocontrol efforts by using a compound like sulfoxaflor that has less impact on beneficial predatory beetles and mites, and parasitic wasps, helps to reduce treatment needs for later season damaging pests such as armyworms, spider mites and aphids.

Sulfoxaflor is expected to become a valuable tool in Integrated Pest Management programs for both major and minor crops. It will replace applications older chemistries which present a greater risk to human health and also may pose a higher ecological risk to non-target organisms, including pollinators. For these reasons, EPA believes it is in the public interest to register sulfoxaflor.

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[9] http://learningstore.uwex.edu/assets/pdfs/A3179.pdf

[10] http://www.extension.umn.edu/garden/insects/find/lawn-and-turf-insects/tables/

[11] http://cropwatch.unl.edu/insect/wheataphids

[12] https://www.epa.gov/sites/production/files/2014-04/documents/pr2001-5.pdf

[13] EPA-HQ-OPP-2010-0889, comment 59, 62, 266, 278

Proposed Registration Decision

EPA is proposing to grant unconditional registrations for sulfoxaflor under section 3(c)(5) of FIFRA. EPA evaluates whether a pesticide will not cause unreasonable adverse effects on man or the environment by taking into account the economic, social, and environmental costs and benefits of the use of the pesticide. EPA is charged with balancing the uncertainties and risks posed by a pesticide against its benefits.

In the case for the proposed use of sulfoxaflor on crops, turfgrass and ornamentals, and in consideration of all best available data and assessment methods, EPA believes this proposed decision to register these uses meets the requirements of FIFRA described above.

The database submitted to support the assessment of human health risk is sufficient for a full hazard evaluation and is considered adequate to evaluate risks to infants and children. The Agency has not identified any risks of concern in regards to human health, including all population subgroups, or for occupational handlers. The assessment is conservative and unrefined.

The ecological risk assessment is conservative and overall presents a low risk to aquatic and terrestrial organisms. The formulated products are short-lived in the field, and present low residual toxicity to beneficial insects. There is no on-field exposure expected to bees for all use patterns since applications will only be made after bloom is completed for bee-attractive crops. All other proposed crops are either not attractive or are harvested before bloom. Off-site exposure and risks to bees appear limited both spatially and temporally. While EPA's "Guidance for Assessing Pesticide Risks to Bees" suggests submission of chronic Tier 1 data on bees is beneficial to a comprehensive risk assessment for bees, such data are not currently required under EPA's regulations. Given the application restrictions on the uses being proposed, the limited exposure to bees associated with them, and a bounding analysis of potential chronic risks to individual bees, EPA has determined these data are not necessary at this time.

As described above, EPA believes registering sulfoxaflor is beneficial because it is being proposed for use on numerous minor use crops and will offer those growers a tool with less toxicity to replace chemicals that are of continuing concern to the Agency. It will support production of many vulnerable crops and the industries that rely on them. With the novel mode of action, sulfoxaflor would become an important part of resistance management strategies for target pests that pose significant threats to many high value crops. Finally, the chemical profile has favorable attributes (i.e., the chemical is not persistent in the field, it's soft on beneficial insects, and has a narrow target pest spectrum) for integration into IPM programs. Sulfoxaflor does not share a common mechanism of toxicity with other chemicals and therefore does not present a cumulative risk to human health unlike alternative organophosphates and carbamates. Another alternative pesticide group, pyrethroids, are widely used and known to have effects on aquatic invertebrates, they are labeled as extremely toxic. In comparison, the acute and chronic risk of sulfoxaflor on aquatic invertebrates is below the level of concern.

The minimal risks of concern have been weighed against the benefits of the proposed uses of sulfoxaflor. EPA finds that registering these uses will not generally cause unreasonable adverse effects on human health or the environment. EPA concludes that the available data and scientific assessments as well as the overall considerations for benefits for protection of high value and important crops support a FIFRA Section 3(c)(5) registration finding for the proposed uses on barley, triticale and wheat; leafy vegetables and watercress; bulb vegetables; canola; fruiting vegetables; root and tuber vegetables; pome and stone fruit; berries; succulent and dry beans; tree nuts; ornamentals and turfgrass (commercial sod farms).

Specifically addressing the Ninth Circuit Court of Appeals' direction to "obtain further studies and data regarding the effects of sulfoxaflor on bees as required by EPA regulations," EPA finds that given the parameters of this proposed decision, there is no need for additional data to be submitted. Further the data requirements found in 40 CFR 158.630 pertaining to insect pollinator testing have been fulfilled. With the amended labels, the use pattern essentially results in no on-field exposure. Indeterminate-blooming crops are not proposed for registration. The remaining sites are either not attractive, harvested before bloom or only receive applications when bloom is over. This mitigation is protective of bees because they would not be foraging on the treated fields. Furthermore, the limited exposure expected from spray drift does not trigger any additional data requirements.

The risk assessments and other background documents for this proposed decision, including cited comments, can be found in docket #EPA-HQ-OPP-2010-0889 at http://www.regulations.gov/#!home.

Public Comment Requested

In addition to requesting comment on the proposed registration of sulfoxaflor, EPA is also seeking public comment on two additional restrictions:

1. Off-site Risk to Pollinators

Although the proposed Transform and Closer labels include mitigation measures that will reduce spray drift, there is a potential for acute risks to bees foraging adjacent to the treated fields if there is blooming vegetation bordering the field downwind. The acute risk is limited to 1 – 12 feet beyond the treated field. The risk finding conservatively assumes that bees are foraging immediately adjacent to the treated field and that they would obtain 100% of their diet from these areas, which is highly unlikely. Estimating off-site chronic risk is somewhat uncertain, but a bounding analysis indicates a potential for chronic risks from 2-49 feet downwind of the treated field. However, this bounding analysis conservatively assumes that bees would obtain 100% of their diet from blooming plants inhabiting this narrow spray drift zone during the time of pesticide application. From a colony perspective, honey bees are known to forage over long distances from the hive (up to 5 miles) and from a wide variety of floral resources. The duration of the estimated chronic risk to bees also appears limited since sulfoxaflor is not persistent in pollen and nectar. If an individual bee is subjected to chronic exposure in this scenario, EPA

believes the benefits of sulfoxaflor outweigh the potential risks. Nevertheless, in order to further protect these foragers from acute exposures, an in-field buffer is proposed to be required. EPA is seeking comment on the following proposed restriction:

- A downwind 12-foot on-field buffer when there is blooming vegetation bordering the field

2. *Uncertainty in Potential Synergistic Effects related to Tank-mixes*

A common agricultural practice involves tank mixing of pesticides, resulting in the co-occurrence of multiple chemical stressors to target pests. The practice of tank mixing can result in significant economic benefits to the grower by allowing control of a wider variety of pests in a single application without incurring the expense of sequential applications. Additionally, by reducing the number of visits to the agricultural field, the grower is also reducing fossil fuel use and emissions from large agricultural equipment, as well as the potential exposure to pesticides that can result from multiple visits to the same area being treated. It is also widely accepted that the practice of mixing products with different modes of action is essential to the management of insect resistance. Because insect resistance is known to have a very costly impact to overall crop yields, which in turn negatively impacts growers' harvests and the price of commodities to the consumer, tools that aid in the prevention of resistance are considered to be a very important benefit to agriculture.

Recently, in some cases, chemical companies have made claims that certain mixtures elicit enhanced activity or synergistic effects, meaning that when the chemicals interact, the overall effect is greater than the sum of the individual effects of each chemical. In EPA's risk assessments, the Agency uses Good Laboratory Practice (GLP) guidelines to determine potential toxicity of individual active ingredients to non-target organisms. EPA believes this approach is very reliable for these purposes. Currently EPA does not require GLP studies for tank mixes suggested on the proposed product label, under the assumption that synergism is not occurring and that following the most restrictive limitations of each product in combination is adequate to mitigate any potential risks associated with the tank mixture. However, if there is evidence to suggest that there are potential synergistic effects, EPA may require such data since the current database for the individual chemicals may not provide adequate information on the risk to non-target organisms from such combinations.

At this time, the topic of synergy and multiple stressors is an uncertainty in assessing risk with tank-mix combinations. EPA must weigh this uncertainty against the benefits of applying tank mixes when considering a regulatory decision. Therefore, EPA is considering whether restrictions on tank-mixing sulfoxaflor are necessary to prevent unreasonable adverse effects, and is inviting comments on the issue of synergism and the potential for tank mix restrictions, which will be taken into further consideration for the final risk-benefit analysis of sulfoxaflor.