UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Sulfoxaflor: Response to Public Comments on EPA's "Proposed Registration of the New Active Ingredient Sulfoxaflor for Use on Multiple Commodities, Turfgrass, and Ornamentals" (Docket # EPA-HQ-OPP-2010-0889)

1) Conditional registrations

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Once again EPA is proposing to repeat missteps of the past by registering a pesticide known to be toxic to non-target organisms without all required data to ensure its safety. As already seen with the neonicotinoid, clothianidin, and the herbicide aminocyclopyrachlor (Imprelis®), conditional registration without relevant ecological data can be detrimental to non-target species. It was pointed out to the agency in previous communications, risks to honey bees far outweigh any economic, social or environmental benefit of conditional registration, given that the honey bee has a $15 billion impact on the agriculture sector and that millions of dollars are at stake for commercial beekeepers, not to mention the economic and environmental costs to native, wild pollinators.

Like clothianidin, we believe any conditional registration of sulfoxaflor is a violation of the terms set out in Section 3(c)(7)(A) [sic], in that registration will pose "unreasonable adverse effects on the environment." The *Federal Insecticide Fungicide and Rodenticide Act* (FIFRA) defines the term "unreasonable adverse effects on the environment" as ''(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide…." EPA has determined that estimated sulfoxaflor residues in pollen and nectar will exceed levels of concern (LOC) for acute risks, but the effects on honey bee colonies are not yet fully understood. Initial tests on brood development were inconclusive. Information on residues and colony health are still outstanding. Given the high uncertainties that remain and initial results that point to high acute hazards, sulfoxaflor presents "unreasonable adverse effects" to bee species, and does not meet statutory standards for registration.

EPA has a long history of registering pesticides without adequately understanding and underestimating human and environmental health impacts. We urge EPA to take a more precautionary approach.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): FIFRA requires a comprehensive set of studies on each pesticide prior to registration. For a Conditional registration, Section 3(7)(c) [sic] of the law states:

> *A conditional registration under this subparagraph shall be granted only if the Administrator determines that use of the pesticide during such period will not cause any*

> *unreasonable adverse effect on the environment, and that use of the pesticide is in the public interest.*

> The information in the docket is not sufficient for the Administrator to draw a definitive conclusion that there will be no unreasonable adverse effects. To the contrary, information EPA does already have suggests that sulfoxaflor is likely to be highly problematic for bees.

EPA's response:

Section 3(c)(7) of FIFRA provides EPA the authority to grant a "conditional registration" for a pesticide product under certain circumstances. The conditions on registrants under this authority involve a requirement to submit particular types of data by a specified date after the registration. In 1978 Congress gave EPA discretionary authority in section 3(c)(7)(C) of FIFRA to approve the registration of a product containing a new active ingredient for which EPA requires additional data, when doing so appeared both to meet the safety standard and to be in the public interest.

Where an application for a new active ingredient lacks some of the necessary data for which there has not been sufficient time to generate and submit since the imposition of the data requirement, EPA may grant a conditional registration under FIFRA 3(c)(7)(C) if EPA determines that 1) during the time needed to generate the necessary data, the pesticide will not cause unreasonable adverse effects on the environment; and 2) use of the pesticide is in the public interest.

EPA proposed on January 14, 2013 to grant a conditional registration under FIFRA 3(c)(7)(C), intending to require data to resolve any residual uncertainty on the potential effects of sulfoxaflor on brood development and long-term colony health at the maximum application rate originally proposed by the registrant and to determine whether this rate can be allowed in the future. After review of the public comments and further consideration of the database, EPA has concluded that an unconditional registration of sulfoxaflor, with lowered application rates and other mitigation is supported by the available data and therefore the appropriate regulatory decision.

EPA disagrees with the assertion that there is inadequate understanding of sulfoxaflor and that the human and environmental health impacts are underestimated. EPA conducted an extensive analysis of sulfoxaflor in collaboration with counterpart agencies in Canada and Australia. Scientists from all three authorities reviewed over 400 studies, peer reviewed the primary evaluations conducted by their international colleagues, and communicated extensively on specific disciplines and issues. Additional EPA committees further reviewed the work done under the joint review project.

Upon completion of the partnered international evaluation of the data, EPA specifically addressed risks to bees in the environmental fate and ecological risk assessment. EPA clearly documented the properties of sulfoxaflor that render it a potential concern to bees: high acute oral toxicity, foliar spray application on pollinator attractive crops, and systemic uptake in plants. Accordingly, EPA conducted a Tier 1 ecological risk assessment to characterize the potential risk concerns. As indicted in the response to comment category #5 below, EPA's Tier 1 ecological risk assessment indicated exceedence of the acute risk level of concern (RQ > 0.4) in only 4 of the 100+ residue samples taken for sulfoxaflor in nectar (the dominant route of oral exposure for foraging bees). Two of these samples were from the highest proposed application rate (0.134 lb a.i./A), which has subsequently been reduced to a maximum of 0.086 lb a.i./A. At 0.086 lb a.i./A and below, only two of the 100+ residue samples have detectable levels of sulfoxaflor that exceed the LOC of 0.4.

Of the six colony-level (Tier 2) toxicity studies available for sulfoxaflor, EPA notes that <u>none</u> of these studies demonstrated a substantial treatment-related decline in colony strength (a key indicator of overall colony health) following confined exposure of bees to sulfoxaflor foliar spray applications. EPA further notes that due to uncertainties associated with the application rates used in these studies and the aforementioned results from the Tier 1 risk assessment, EPA proposed reducing the maximum application rate of sulfoxaflor from 0.134 lb a.i./A to 0.086 lb a.i./A. This lower maximum application rate was evaluated in two of the available semi-field studies. Notably, the cotton tunnel study, which includes the maximum seasonal rate of 0.266 lb a.i./A, indicated that colony strength was similar across all treatments relative to pre-application conditions of the hives.

Consistent with the conclusions of the joint review project and EPA's risk assessment, the Pesticide Registration and Control Division of the Department of Agriculture, Food & the Marine in Kildare, Ireland, serving as the rapporteur member state for the European Union, reported on their summary, evaluation and assessment of sulfoxaflor. Regarding potential risks to bees, they stated that no unacceptable acute or chronic effects on colony survival and development were noted. They concluded that the risk to bees from the proposed uses of sulfoxaflor and its formulated products is acceptable.

2) Resistance concerns and alternative pesticides

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): While surveys have shown neonicotinoid resistance to still be restricted to very few species and often very localized in extent,[1] it is predictable that the widespread use of neonicotinoid insecticides will continue to give way to increased insect resistance. There is reported imidacloprid resistance in certain aphid species, with cross-resistance to other neonicotinoids.[2] One study documented acetamiprid, clothianidin and thiamethoxam resistance at 6.4, 10, and 22-fold, respectively in cotton aphids (*Aphis gossypii).*[3] High levels of cross-resistance to thiamethoxam, imidacloprid, and acetamiprid have also been detected in silver whitefly (*B. tabaci*).[4] Insects with neonicotinoid resistance have also been shown to have varying resistance to organophosphates, carbamates, and pyrethroids.[5] Due to growing resistance among insect populations, stronger pesticides with novel mode of actions are being sought. In the case of sulfoxaflor, it is stable in the presence monooxogenase enzymes –responsible for metabolizing chemicals and known to be involved in resistance to the neonicotinoids and other insecticides[6]- making sulfoxaflor a more potent insecticide to the insect. Industry is advertising sulfoxaflor as a "critical tool for insect resistance management," due to its new mode of action and its effectiveness on insect populations resistant to neonicotinoid and other insecticides.[7]

According to some industry scientists, sulfoxaflor has a pharmacological profile (in aphids) consistent with that of imidacloprid, suggesting that sulfoxaflor be considered a neonicotinoid.[8] However, others

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[1] Nauen, R and Denholm, I. 2005. Resistance of Insect Pests to Neonicotinoid Insecticides: Current Status and Future Prospects. Archives of Insect Biochemistry and Physiology 58:200–215

[2] Nauen R, Vontas J, Kaussmann M, Wölfel K. 2012. Pymetrozine is hydroxylated by CYP6CM1, a cytochrome P450 conferring neonicotinoid resistance in Bemisia tabaci. *Pest Manag Sci*. 2 doi: 10.1002/ps.3460

[3] Herron, G. A. and Wilson, L. J. 2011. Neonicotinoid resistance in *Aphis gossypii* Glover (Aphididae: Hemiptera) from Australian cotton. Australian Journal of Entomology, 50: 93–98.

[4] Nauen, R and Denholm, I. 2005. Resistance of Insect Pests to Neonicotinoid Insecticides: Current Status and Future Prospects. Archives of Insect Biochemistry and Physiology 58:200–215

[5] Nauen, R and Denholm, I. 2005. Resistance of Insect Pests to Neonicotinoid Insecticides: Current Status and Future Prospects. Archives of Insect Biochemistry and Physiology 58:200–215.

[6] Sparks, T, DeBoer, G, et al. 2012. Differential metabolism of sulfoximine and neonicotinoid insecticides by *Drosophila melanogaster* monooxygenase CYP6G1. Pest Biochem. Phys. 103 (2012) 159–165

[7] Annetts, R and Elias, N. 2012. Sulfoxaflor For Management Of Cotton Pests In Australia. Presented at the *Australian Cotton Conference*, Management of Cotton Aphids. Available at http://www.australiancottonconference.com.au/2012-presentations-papers/annetts-robert

[8] Cutler P, Slater R, Edmunds AJ et al. 2012. Investigating the mode of action of sulfoxaflor: a fourth-generation neonicotinoid. *Pest Manag Sci.*

at Dow AgroSciences laboratories argue that the very high efficacy at nAChRs, coupled with its chemical structure, lack of cross-resistance, and metabolic stability,[9] prove that sulfoxaflor is a novel insecticide. Sulfoxaflor has been demonstrated to exhibit very low resistance in some aphid species (e.g. silverleaf and greenhouse whiteflies) already resistant to imidacloprid with no evidence of cross resistance to other neonicotinoid pesticides, making it a good candidate to control pests already resistant to certain neonicotinoids.[10] [11] One study investigating the efficacy of sulfoxaflor in the field, determined that sulfoxaflor proved to be more "residual and significantly more potent," even with similar speed of action when compared to neonicotinoids.[12]

The evolution of insect resistance is predictable, leading to farmers resorting to multiple chemicals, alternating insecticides with different modes of action (which would have to be either more toxic, or used in greater frequency), in order to control resistant insects. However, the risks to non-target insects in the advent of failed technologies are not seriously considered.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): Sulfoxaflor should be considered a subcategory of the neonicotinoid class of insecticides rather than the first member of the sulfoximine insecticide class based on its similarities in mode of action and its structure that mimics the neonicotinoid toxicophore. This classification should be taken into account for insecticide resistance management plans.[13] While the applicant, Dow AgroSciences, has asserted in published literature that sulfoxaflor is the first insecticide in the new sulfoximine class of chemicals[14] (distinct from the neonicotinoids), other assessments of the compound suggest that it may instead be a new subclass of the neonicotinoids.[15] EPA refers to sulfoxaflor as "the only member of the sulfoxamine subclass of neonicotinoid insecticides" in the beginning of its RA, but later mentions that it is distinct from the neonicotinoids for insecticide resistance management.[16] EPA should resolve this confusion and clarify that sulfoxaflor is a subclass of neonicotinoids in light of the conflicting information from the applicant and the agency.

An investigation of sulfoxaflor's mode of action found that it interacts with the high-affinity imidacloprid binding site in the insect's nAChR.[17] Sulfoxaflor also behaves in a method similar to imidacloprid *in situ* in aphids at both the receptor and neuronal levels.[18] These characteristics could pose problems for cross-resistance with neonicotinoids, and should be factored into insecticide resistance management plans. Most of the currently-identified resistance to commercialized neonicotinoids is caused by enhanced monooxygenase metabolism.[19] Sulfoxaflor is stable to monooxygenases, so it can control pests that have developed metabolic resistance to the neonicotinoids.[20] However, resistance can also be conferred by a target site mutation that sulfoxaflor

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doi: 10.1002/ps.3413.

[9] Watson GB, Loso MR, Babcock JM, et al. 2011. Novel nicotinic action of the sulfoximine insecticide sulfoxaflor. *Insect Biochem Mol Biol.* (7):432-9.

[10] Longhurst C, Babcock JM, Denholm I, Gorman K, Thomas JD, Sparks TC. 2012. Cross-resistance relationships of the sulfoximine insecticide sulfoxaflor with neonicotinoids and other insecticides in the whiteflies Bemisia tabaci and Trialeurodes vaporariorum. *Pest Manag Sci*. doi: 10.1002/ps.3439.

[11] Siebert, M, et al.2012. Field Evaluations of Sulfoxaflor, a Novel Insecticide, Against Tarnished Plant Bug (Hemiptera: Miridae) in Cotton . *J Cotton Science 16:129–143*

[12] Lysandrou, M, Ahmad, M and Longhurst, C. 2010. Comparative Efficacy Of Sulfoxaflor Against Cotton Leafhopper, *Amrasca Devastans* (Distant) (Cicadellidae: Homoptera) Under Field Conditions Of Punjab And Sindh. *J. Agric. Res*.48(4)

[13] Cutler P, et al. 2012. Investigating the mode of action of sulfoxaflor: a fourth-generation neonicotinoid. *Pest Manag Sci*. doi: 10.1002/ps.3413.

[14] Babcock JM, et al. 2010. Biological characterization of sulfoxaflor, a novel insecticide. *Pest Manag Sci*. 67(3): 328-334.

[15] Cutler P, et al. 2012.

[16] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 8.

[17] Cutler P, et al. 2012.

[18] Cutler P, et al. 2012.

[19] Babcock JM, et al. 2010.

[20] Cutler P, et al. 2012.

was susceptible to in trials, a type of resistance that is not discussed in the RA's discussion of cross-resistance.[21] [22] The levels of resistance to sulfoxaflor identified in strains with target-site mutations could have a major impact on field performance of these products.[23] Sulfoxaflor's mode of action is not yet fully understood, and initial results show some cross-resistance with neonicotinoids, which should lead to their categorization as neonicotinoids to manage insecticide resistance. The concerns about potential cross-resistance with commercial neonicotinoids should be further explored, and are not addressed adequately in the evaluation of sulfoxaflor's proposed registration.

David Kerns' (LSU AgCenter) comment (Docket # EPA-HQ-OPP-2010-0889-0059): Based on my evaluations, sulfoxaflor appears to have an excellent fit in the Mid-South's cotton production system; having excellent efficacy towards tarnished plant bug, cotton fleahopper and cotton aphid. Additionally, the use of sulfoxaflor as an alternative to a number of insecticides currently used for plant bug management should help alleviate problems associated with destruction of natural enemies, pest resurgence and secondary pest outbreaks.

The Mid-South cotton producing states including Tennessee, Arkansas, Mississippi and Louisiana have had extremely difficult problems effectively controlling tarnished plant bug in cotton, and subsequent secondary pest outbreaks. Tarnished plant bugs are a key pest of cotton and have been the number one yield limiting pest for more than 10 years. Plant bugs damage cotton primarily by feeding on the squares (flower buds) causing them to abort. Thus the fruit is lost resulting in a reduction in lint. Tarnished plant bugs are usually most abundant once the cotton crop begins to flower, and they will remain potential pests until all of the harvestable fruit are set. Thus it is imperative that cotton be protected from excessive plant bug injury from square formation until crop cutout.

Growers utilize a number of integrated approaches for managing plant bugs in cotton including: planting more tolerant varieties, landscape manipulated to avoid placement of cotton adjacent to corn, managing weeds that host plant bugs, and utilizing insecticides. The insecticides used for managing plant bugs in cotton rely heavily on organophosphates and neonicotinoids. Due to resistance issues we have seen a shift to acephate synergized with pyrethroids, and neonicotinoid/pyrethroid mixtures. These mixtures have been effective but short lived; when immigrating plant bug populations are high, it is not uncommon to have to retreat fields within 5 days. Cotton growing in areas with naturally high plant bug populations in the landscape may require as many as 10 insecticide applications during a year.

Unfortunately these insecticides have detrimental effects on arthropod natural enemies leading to outbreaks of secondary pests. Acephate is notorious for flaring spider mites, and pyrethroids are notorious for flaring spider mites and aphids. Thus, follow up applications of miticides or aphicides are often necessary following insecticide applications targeting plant bugs. Some of the neonicotinoids have proved efficacious towards aphids, but in recent years resistance to most of these products has been widespread. Additionally, the neonicotinoids were once thought to have marginal impact on arthropod natural enemies, but in research I have conducted over the past 4 years, I have found these products to be extremely harmful towards lady beetle larvae. Therefore, not only are we seeing aphids develop resistance to some neonicotinoids, but these same products are destroying the aphid's natural enemies. Sulfoxaflor however, is one of the best aphicides I have evaluated, and thus

[21] Cutler P, et al. 2012.
[22] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 14.
[23] Cutler P, et al. 2012.

flaring aphids would not be likely. Additionally, I was suspicious that sulfoxaflor, because it has a similar mode of action to the neonicotinoids, might also be harsh on lady beetle larvae, but this has not been the case. My data suggests it is much softer than any of the neonicotinoids I have tested. In many respects sulfoxaflor appears to be very different from the neonicotinoids, not only in its lesser impact on arthropod natural enemies, but research has demonstrated that aphids resistant to neonicotinoids are not cross resistant to sulfoxaflor.

Without access to new and improved insecticide chemistries to manage our insect pests we will only see increased reliance and use of the older, harsh insecticide chemistries; and continuation of the insecticide treadmill. Sulfoxaflor could replace a number of harsh insecticide applications with a product that is highly effective towards the target pests, safer towards a number of the key natural enemies, and much less likely to cause secondary pest outbreaks. These characteristics would make sulfoxaflor an excellent candidate for managing pests in Mid-South cotton, and ultimately becoming a cornerstone of a much more robust and effective cotton IPM program.

Elizabeth Beers' (WSU) comment (Docket # EPA-HQ-OPP-2010-0889-0266): As an industry, we have been relying solely on the neonicotinoid insecticides (IRAC Group 4A) for aphid control for nearly two decades. The extension of their spectrum into our key lepidopteran pests has increased the overall numbers of applications per season, without any rotational materials to fit into a resistance management plan. New modes of action are needed for these pests. In addition, the neonicotinoids are weak against one of more troublesome aphid species, woolly apple aphid. Unlike other aphid species, this pest causes chronic debilitation of the tree, and fruit contamination is cited frequently as a cause for rejection or fumigation of exported fruit. The last two conventional materials that were effective (endosulfan and diazinon) are being phased out, leaving a serious gap in our programs; sulfoxaflor is one of the few materials I have tested in the last 10 years that can control woolly apple aphid. Materials such spirotetramat provide a prophylactic alternative, but do not allow as much flexibility in IPM programs. For these reasons, I am happy to support the registration of sulfoxaflor in the tree fruit market.

Scott Stewart's (University of Tennessee) comment (Docket # EPA-HQ-OPP-2010-0889-0266): Given well established and increasing resistance to alternative insecticides, sulfoxaflor has a real fit in managing infestations of tarnished plant bugs and cotton aphids. Sulfoxaflor represents a new mode of action that will replace applications of neonicotinoid, pyrethroid, and organophosphate insecticides. Many of my efficacy trials with sulfoxaflor are available on the internet at http://www.utcrops.com/MultiState/MultiState.htm (or upon request). My testing indicates that sulfoxaflor provides control of tarnished plant bugs and cotton aphids that is equal to and typically superior to alternative insecticide. Thus, I expect sulfoxaflor to reduce the total number of foliar application needed to control insect pests in cotton.

Growers in the Midsouth have a critical need for new modes of action that control resistant insects and maintain profitability by providing better crop protection with fewer insecticide applications. Compared with many alternative insecticide options, the data suggests that sulfoxaflor is relatively "soft" on beneficial insect populations in cotton, and this may prevent additional applications targeting secondary pests such as spider mites and cotton aphids. Of course, the effects of insecticides on pollinators have been front and center during the last year. It has been suggested that the use of sulfoxaflor use be to the pre-flowering window in cotton to limit exposure to pollinators. This would greatly limit the potential benefits of this insecticide. The greatest need for plant bug control occurs during the blooming window, and frankly, I know of no reason to believe sulfoxaflor has any greater effect on pollinators than alternative insecticides. Indeed, I suspect the opposite, particularly given the rigorous scientific scrutiny applied during the registration process.

Tennessee utilized a limited amount of sulfoxaflor in 2012 under a Section 18. Growers and consultants were impressed with its performance in controlling tarnished plant bugs and protecting yield. I received no reports of performance failures, secondary pest outbreaks, bee kills or other negative effects. The data available indicates that sulfoxaflor is a relatively benign insecticide that represents a substantial improvement over alternative insecticides. I think the registration of sulfoxaflor will represent a step forward for both cotton producers and for "environmental health".

Roy Parker's (Texas A&M) comment (Docket # EPA-HQ-OPP-2010-0889-0210): Sulfoxaflor (Transform) has been included in my field studies on cotton during each of the past three years primarily for the control of cotton fleahopper and cotton aphid. In those studies I found it to be very effective in keeping the fleahopper below economic injury level with performance equal to the neonicotinoids and organophosphates. In addition, the chemistry provided outstanding control of the cotton aphid. The combination of effective fleahopper and aphid control provides an advantage in that treatment for the fleahopper does not result in resurgence of cotton aphis. Therefore, it has a good fit in an integrated pest management program by reducing the needed to apply an additional treatment for cotton aphid at a later date. Although some of the neonicotinoids also provide similar aphis control (recuded potential for aphis increase), the availability of the different mode of action provided by sulfoxaflor allows us to use different chemistry in cotton where neonicotinoids are being used extensively. We need this different mode of action available as an insecticide resistance management tool.

My studies demonstrate that one to three treatments for the cotton fleahopper are required from initiation of squaring (bud formation) through the first week of bloom. In some years, depending upon growing conditions, cotton lint yields are greatly enhanced by control of the cotton fleahopper.

Western Growers' comment (Docket # EPA-HQ-OPP-2010-0889-0362): Some of the products our industry has relied on for years to control aphids have either been phased out or restrictions have been added to labels making them more difficult to use. The registration of new, effective aphid control products is critical for continued production of these crops. Research data from University of California and University of Arizona demonstrate that Closer Insecticide provides excellent control of all aphid species damaging cole crops and leafy vegetables. Closer is used at a very low use rate. The proposed use parameters such as the pre harvest interval and restricted entry interval for this product are very compatible with the production systems used by our grower members.

Another key pest in leafy vegetables, cole crops as well as melons and fruiting vegetables is whitefly. Whitefly feeding produces honeydew which can make harvest difficult and reduce quality. Whitefly also transmits plant viruses which can dramatically reduce crop yield and quality. Effective control of whiteflies is a must for producing high quality crops, especially in desert production areas where whitefly populations can be very damaging. Whiteflies have demonstrated an ability to develop resistance to insecticides very quickly so it is important to have multiple modes of action available. Research data from University of Arizona has shown that Closer is effective in controlling whitefly and has been demonstrated to reduce virus incidence in fall melons.

Due to restrictions and removal of some key insecticides in strawberries such as Lannate (methomyl), insect pest management has become more challenging. One of the most serious pests is Lygus. This insect can cause great losses for strawberry growers from feeding on developing flowers resulting in malformed fruit which is unmarketable. Left untreated, losses of greater than 50% of the crop are possible. Research trials conducted in 2012 by the CA Strawberry Commission in conjunction with University of California demonstrated significant increases in marketable yields. Closer will be a critical tool for growers in controlling this challenging pest.

We understand that some crops have language restricting use during and around bloom. In crops like melons and strawberries bloom occurs early and throughout a large part of the life cycle of the plant. Therefore, it is critical to have flexible application restrictions to be able to effectively use this and other products. The insect control spectrum of Closer paired with its unique mode of action make it an important new tool for our growers.

Anonymous extension entomologist's (MSU) comment (Docket # EPA-HQ-OPP-2010-0889-0062): I am an Extension Entomologist at Mississippi State University with statewide responsibilities in cotton, corn, soybean, wheat, and grain sorghum. I have tested Sulfoxaflor extensively over the last several years in cotton against tarnished plant bugs and cotton aphids. Tarnished plant bugs are the number one insect pest of cotton in Mississippi often requiring 8-12 applications for this pest alone in the Delta region of the state. This is due to widespread resistance to other classes of chemistry. Sulfoxaflor offers producers a new mode of action to rotate into their management program that will replace neonicotinoid applications prior to bloom and organophosphate applications after bloom with increased efficacy over existing products which possibly may further eliminate follow up applications with less efficacious products. Also, because this product is equally effective on cotton aphids, it will save one application of a neonicotinoid when both pests are present at the same time since Mississippi no longer has effective insecticides that control tarnished plant bugs and cotton aphids at the same time.

It is critical to producers in Mississippi and the Mid-Southern area that they have access to new modes of action to control resistant insects such as tarnished plant bugs and cotton aphids season long. It needs to be further emphasized that use of this product will not add additional applications but rather replace older more harsh chemistry. I have seen the beneficial insect profile from entomologist at other universities and it has much less impact on the beneficial insects present in cotton which again may further reduce total insecticide usage. Furthermore, I realize that there is some concern with bee keepers anytime a new insecticide is released. However, any new insecticide that is released today undergoes much more scrutiny and testing as new scientific testing procedures are developed and incorporated into the registrant's application process. Again, because this is a new compound that has proven to be a "softer" chemistry on beneficial insects and bees it will replace applications of older chemistry that is much more disruptive to the system. This should be viewed as positive benefit to the whole industry.

Larry Godfrey's (UC Davis) comment summary (Docket # EPA-HQ-OPP-2010-0889-0278): Sulfoxaflor, based on my research, appears to be uniquely situated to contribute positively to integrated pest management programs of cotton in California. The pest spectrum of sulfoxaflor, western tarnished plant bugs (Lygus hesperus) and cotton aphids (Aphis gossypii), represent two of the most damaging and economically-concerning pests of cotton. Based on annual estimates of cotton crop losses made by cotton entomologists in California (as well as in other states), L. hesperus generally causes the greatest yield loss among arthropod pests of cotton in California. Depending on the year, up to a 5% loss is recorded in spite of the use of recommended management practices. This pest infests numerous crops in the San Joaquin Valley (SJV) and flourishes in the intensive agriculture of this production area. IPM specialists have developed a well-balanced program for managing L. hesperus in cotton utilizing cultural controls, biological controls, a vigorously-growing/well-managed cotton crop, but insecticides are still needed to prevent economic losses in the cotton crop. The dynamic nature of this pest and intricacies of this production system mean that non-chemical methods alone are not sufficient. During my 20-year career, cotton growers have relied on carbamate, organophosphate, and pyrethroid insecticides for lygus management. The former two classes of chemistry have largely been removed from the “toolbox” due to insecticide resistance in L. hesperus and regulatory actions with the loss of aldicarb (Temik®) being the most recent action. Pyrethroid insecticides have been used for the last ~15 years and were the standard insecticide treatment for lygus in the SJV. This class of chemistry “stressed” the IPM programs due to their broad-spectrum nature and propensity to kill natural enemies which promoted populations of cotton aphids (therefore creating a secondary pest and additional insecticide applications). Insecticide resistance is presently developing to lygus bugs in the San Joaquin Valley to pyrethroid insecticides and growers are in need of alternative insecticidal approaches. Flonicamid was registered ~5 years ago and is presently very effective against lygus bugs in cotton and heavily used by cotton growers. Resistance to this active ingredient has not yet been detected but having insecticide rotational partners such as sulfoxaflor is the optimal scenario in order to provide sustainable IPM programs, i.e., protect all available effective chemistry from the development of resistance.

A. gossypii, the other primary target of sulfoxaflor in the SJV, while also potentially reducing lint yield, has the most potential to negatively impact cotton lint quality. During the period of open lint, feeding by aphids potentially results in honeydew deposition on the lint which reduces the quality and ability to process the lint. In the worst case scenario, a production region gains the reputation of producing “sticky cotton” and long-term ramifications on marketability of the cotton can result. Presently in the SJV, cotton aphid management relies on applications of chlorpyrifos and neonicotinoid insecticides. During the late-season period (August to harvest), my research has shown the aphid threshold for sticky cotton is very low (5 to 10 aphids per leaf), so growers pay close attention to management of this pest. Both of these insecticides are under scrutiny with chlorpyrifos use being examined due to water quality issues. In addition, aphid resistance to the neonicotinoid insecticides is widespread in Mid-South cotton and, given 15 years of use in the SJV, is likely to occur or perhaps already present at some level. Flonicamid is also highly effective against cotton aphids but this insecticide is generally “reserved” for use against lygus bugs (or has already been used during the season prior to the need for cotton aphids which generally infest ~4-6 weeks after lygus bugs).

Sulfoxaflor has less impact on populations of natural enemies than the other insecticides used for lygus bug management (pyrethroids) and protecting these beneficials helps to keep other arthropod pest populations in check (late-season spider mites, beet armyworms, whiteflies, etc.). This helps to reduce treatment needs for these pests. Finally, sulfoxaflor in my research has provided excellent protection of cotton yields which will promote the profitability of cotton and its role in the agricultural economy.

Beth Grafton-Cardwell’s (UC Riverside) comment (Docket # EPA-HQ-OPP-2010-0889-0161): I have conducted a research and extension program for 23 years on the subject of integrated pest management of citrus pests in the San Joaquin Valley of California. U have worked with sulfoxaflor since 2009 and studied its impact on a key pest of citrus, the citricola scale, *Coccus pseudomagnoliarum*. Currently, citricola scale is controlled primarily with the organophosphate insecticide chlorpyrifos. Reliance on chlorpyrifos ot manage citricola scale has resulted in the development of resistant populations and new insecticides such as sulfoxaflor are needed as rotational chemistries to control the pest. A single application per year of sulfoxaflor in the rate range of 7.13 to 8.55 oz per acre which is 100-150 gm ai/acre is very effective in controlling citricola scale. Citricola scale often requires a higher concentration of insecticide than other insect pests, because the water volume that is applied to achieve coverage of the tree and ensure contract with the insect is 3—500 gallons per acre. Registration of sulfoxaflor at 8.55 oz/acre will reduce the number of applications of chlorpyrifos used for this pest in the San Joaquin valley. Lower concentrations of sulfoxaflor are likely to require more frequent applications of this or other pesticides to control citricola scale.

Jeffrey Gore (Mississippi State Univ) comment (Docket ID No. EPA-HQ-OPP-2010-0889-0308): The purpose of this letter is to support the registration of sulfoxaflor, a new insecticidal active ingredient. I am an assistant professor at the Mississippi State University, Delta Research and Extension Center in Stoneville, MS. I am an Entomologist with responsibilities for insect control in row crops grown in Mississippi. Currently, producers in the midsouthern U.S. face numerous challenges in crop production. Weed and insect species that have developed resistance to numerous pesticides have created a unique challenge that threatens the economic viability of many growers. In relation to sulfoxaflor, cotton producers in Mississippi have two important insect pest species that are resistant to most of the insecticides currently labeled for their control. The tarnished plant bug, *Lygus lineolaris,* has become the most important insect pest of cotton in the Mid-South. Growers in my region of Mississippi generally make 5-12 applications annually targeting this insect. The development of resistance to pyrethroids, organophosphates, and carbamates in the tarnished plant bug is the most important cause for the increased numbers of applications targeting this insect. Currently, the neonicotinoid class of insecticides and the insect growth regulator, novaluron, are the only effective insecticides for which resistance has not been documented in tarnished plant bug. As a result, cotton growers in Mississippi have had to rely heavily on insecticides in the neonicotinoid class and the frequency of applications with neonicotinoids has increased in recent years. Coincidentally, the increased frequency of neonicotinoid applications targeting tarnished plant bug has inadvertently selected for cotton aphid population with high levels of resistance to this insecticide class. The only effective insecticide labeled for cotton aphid control is the pyridine carboxamide, flonicamid.

Another consequence of the increased applications needed to manage insecticide resistant tarnished plant bug is outbreaks of spider mites. Twospotted spider mite has become a season long pest of cotton in Mississippi. The increased incidence of acaricide applications targeting spider mites has coincided with the occurrence of insecticide resistance in tarnished plant bug and there is a strong correlation between the numbers of applications for spider mites and the numbers of applications for tarnished plant bug. Increased applications with high rates of broad spectrum insecticides such as pyrethroids, organophosphates, and neonicotinoids eliminate natural enemy complexes in cotton and create an ideal environment for outbreaks of spider mites. Research by a recent graduate student in Mississippi showed that foliar applications of neonicotinoids, pyrethroids, and organophosphates can flare spider mites in cotton. This has created an additional input cost for growers in the Delta regions of the Mid-South.
I have been testing sulfoxaflor for the last six years in cotton. My research has involved field experiments evaluating the control of both tarnished plant bug and cotton aphid with sulfoxaflor in cotton and comparing it to currently labeled insecticides. Sulfoxaflor has performed well in all of those experiments and is comparable to our current standards. In Mississippi, the current standard for control of tarnished plant bug is 1.0 lbs ai/A of acephate tank mixed with a pyrethroid or 0.05 lbs ai/A of thiamethoxam mixed with a pyrethroid. Sulfoxaflor applied at 0.047 lbs al/A alone has performed as good, or better than these treatments. Similarly, sulfoxaflor applied at 0.023 to 0.047 lbs ai/A has performed better than the currently labeled insecticides against cotton aphid.

The Delta counties of Mississippi were fortunate to be granted a Section 18 for the use of sulfoxaflor in 2012. I was able to view the performance of sulfoxaflor in large field situations and it performed similarly to what I previously observed in small plot replicated trials. Consultants and growers were generally happy with how sulfoxaflor performed on their fields in Mississippi.

> In addition to good control of target pests with sulfoxaflor, there are minimal, if any, non-target effects with this insecticide. In research plots, we have not seen an increased incidence of twospotted spider mite following sulfoxaflor applications. Also, because sulfoxaflor has good activity against both tarnished plant bug and cotton aphid, it will be the only insecticide that will effectively control both species in cotton. Because of these factors, sulfoxaflor is an important insecticide for the future sustainability of cotton production in many areas of the Mid-South. Sulfoxaflor will likely replace 1-2 applications of neonicotinoids during the early season and 1-2 applications of organophosphate/pyrethroid tank mixtures later in the season. Also, because it his little non-target effect and controls cotton aphids, the numbers of applications targeting other arthropod pests may also be reduced. Finally, the selective nature of sulfoxaflor, high level of control against target pests, and low use rates will provide a valuable tool for cotton growers in Mississippi. Sulfoxaflor will allow us to design a more effective insecticide rotation strategy that will minimize the economic impacts of multiple pest species and reduce the selection pressure on other classes of insecticides.

EPA's response:

During the public comment period for this proposed registration decision, EPA received comments supporting the Agency's determination that the benefits of sulfoxaflor outweigh the risks. These comments were from organizations representing numerous growers of a wide variety of crops, including minor use crops. The groups included the California League of Food Processors (0250), Washington State Potato Commission (0275), US Canola Association (0279), the American Soybean Association (0305), the National Sunflower Association (0307), the California Grape and Fruit Trade (0312), the California Specialty Crops Council (0313), the National Cotton Council (0317), the California Strawberry Commission and the United Fresh Product Association (0379). Individual growers also commented, as did a number of researchers who have long studied insecticide resistance management. These researchers not only have expertise in this area but indicated that their careers and livelihood are based on years of studying insecticide resistance management and have personal knowledge of product performance based on their experiences leading research in the field.

As stated by David Kerns (comment #059, above), cotton growers have developed various strategies for combating plant bugs but have had to rely heavily on organophosphates and neonicotinoids, with as many as 10 insecticide applications per year. As stated in his comment, these older chemistries can flare up other target pests resulting in even more pesticide applications. These additional applications would be expected to be harmful to pollinators.

Both Elizabeth Beers (comment #0266) and Roy Parker (comment #0210) believe that sulfoxaflor would be of benefit to growers in targeting pests that have developed resistance to neonicotinoids. Their comments regarding research in this area support the position that sulfoxaflor will fit into IPM programs. This is further supported by the comment from Mississippi State University (#0062) that sulfoxaflor's new mode of action will replace neonicotinoid and organophosphate applications as well as reduce the number of applications of insecticides to cotton.

These comments from researchers, who are actively engaged in pest management research, provide further evidence to EPA's conclusion that sulfoxaflor is different from the registered neonicotinoids. Not all chemicals in the Insecticide Resistance Action Committee (IRAC) Group 4 classification have comparable efficacy on target pests and/or comparable risk to non-target organisms. The primary site of action for Group 4 compounds is the nicotinic acetylcholine receptor. Subclass 4A are the neonicotinoids. Even between this subclass, there are differences. The nitroguanidine subclass is highly toxic to honey bees while the cyanoamidine subclass is relatively nontoxic to honey bees. Group 4C is assigned to sulfoxaflor which presents a different mode of action to the target site and thus appears to be efficacious against some resistant pests. Further, according to commenters # 0059, 0266, 0062, 0278 and 0308, they have seen evidence that sulfoxaflor is softer on beneficial insects than other available pesticides.

The commenter #0363 noted that, while sulfoxaflor activity was not affected by enhanced monooxygenase metabolism, the most common resistance mechanism in insects, there are other resistance mechanisms that can affect the activity of sulfoxaflor. EPA acknowledges that other mechanisms of resistance exist and may affect field performance of sulfoxaflor in the future. Currently, however, these resistance mechanisms are rare in field populations of insect pests and are not responsible for the vast majority of current cases of resistance. Therefore, in the short term, EPA believes that sulfoxaflor's lack of cross resistance will be useful for resistance management purposes. In the longer term, EPA acknowledges that other mechanisms of resistance may impact the performance of sulfoxaflor in the field and may necessitate continued vigilance in resistance management efforts. The Agency does not evaluate compounds based on potential mutations of the target site and future resistance. However, the labels include language regarding Integrated Pest Management (IPM) and Insecticide Resistance Management (IRM), to prevent the potential development of resistance to sulfoxaflor.

3) Sulfoxaflor degradates

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): While sulfoxaflor may biodegrade rapidly in aerobic conditions, its soil degradates are mobile and "expected to be highly persistent in aerobic soil/aquatic systems."[24] [25] Sulfoxaflor and all of its degradates should be included in all of the risk assessment calculations. The major degradate (X11719474 [X-474]) has a different mode of action and is less toxic than sulfoxaflor, but is also systemic and could be absorbed from the soil by target crops, or successive crops in the same fields because of its long half-life.[26] This would be of greater concern and would need to be revisited if a soil-applied use was approved, but is still an issue with the proposed application methods. One of the minor degradates (X11519540 [X-540]) is more toxic than sulfoxaflor but it forms at low concentrations so was mostly excluded from the risk assessments. For aquatic organisms, the RA only evaluated sulfoxaflor and X-540. While EPA asserts that "available evidence indicates that the X-474 degradate does not share the same MOA as the parent and is much less toxic based on measures of effect relevant to ecological risk assessment," this dismissal still represents a significant release of a compound into the environment about which little is known.[27] EPA goes on to state that "X-474 is expected to dominate the exposure resulting from use of sulfoxaflor," suggesting that it is irresponsible to exclude X-474 from both the aquatic and terrestrial RA.[28] The current RA is inadequate to assess the potential risks from the stable X-474 in the aquatic environment. For terrestrial organisms, the RA evaluates parent sulfoxaflor only. Given the rapid biodegradation of sulfoxaflor, and its metabolism into degradates in plant tissue, this is inadequate to protect terrestrial species that may be exposed to residues. The combination of water solubility, persistence, and toxicity (especially to bees and other insect pollinators) is particularly concerning because compounds with these same characteristics have shown adverse effects to non-target species. Sulfoxaflor and its degradates' persistence in the environment is concerning because of the numerous detrimental impacts to non-target organisms that

[24] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 10.
[25] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 37.
[26] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 46.
[27] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 8.
[28] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 10.

have not been fully assessed.

EPA's response:

For sulfoxaflor and other pesticides, identifying residues of concern for ecological risk requires consideration of exposure *and* ecotoxicological effects. As explained on page 17 of the Environmental Fate and Effects Division's assessment, the degradate X-474 is expected to be a "major" degradate (i.e., > 10% formation relative to the parent) in the aquatic and terrestrial ecosystems. However, multiple lines of evidence indicate that the X-474 does not possess the same ecotoxicological concerns as parent sulfoxaflor.

One important line of evidence is available toxicity data which indicates X-474 is "practically non-toxic" to multiple taxa including fish (rainbow trout), aquatic invertebrates (water flea), terrestrial invertebrates (honey bee), birds (bobwhite quail) and mammals (rat).

In addition to the low hazard the X-474 degradate poses to non-target animals, available information indicates the X-474 degradate does not share the same mode of action as parent sulfoxaflor. Empirically, this is demonstrated by the lack of acute toxicity of the X-474 degradate to the honey bee (oral acute LD_{50} > 100 ug a.i./bee) as compared to parent sulfoxaflor (oral acute LD_{50} = 0.13 to 0.38 ug a.i/bee). The minor degradate X-061 is similarly not acutely toxic to honey bee (LD_{50} > 104 ug a.i./bee).

In addition to empirical information, QSAR modeling for X-474 based on ECOSAR v 1.00 confirms its lack of acute toxicity to fish and aquatic invertebrates with predicted acute LC_{50} values of 740 and 240 mg /L respectively, based on the amide ECOSAR chemical class. QSAR modeling also indicates the chronic toxicity of X-474 to fish and aquatic invertebrates is relatively low, with predicted chronic values of 4.4 and 3.1 mg/L, respectively using ECOSAR and the amide chemical class. Chronic estimated environmental concentrations (EECs) for total sulfoxaflor residues (including X-474) are more than 100X below these predicted chronic values, thus indicating a large margin of safety with respect to chronic risk of the X-474 degradate to aquatic animals. Predicted 96-h EC_{50} and long-term toxicity values for green algae using ECOSAR are 1.8 and 0.5 mg/L, respectively, which are an order of magnitude above EECs for sulfoxaflor and all its degradates combined.

Lastly, the Agency notes that in its aquatic ecological risk assessment, it initially conducted a screening assessment by including all degradates of interest for sulfoxaflor in the aquatic EECs (parent + X-474+X-540) for efficiency purposes. As indicated in the Agency's ecological risk assessment document, risk quotients (RQ) based on these degradates of interest were well below acute and chronic levels of concern for fish, freshwater invertebrates and aquatic plants. Therefore, inclusion of the X-474 degradate would not alter the risk conclusions for these taxa. For two taxonomic groups, marginal exceedences of the listed species acute risk LOC of 0.05 and chronic LOC of 1.0 were observed using all of the residues of interest. Further refinement was conducted by including only those degradates of toxicological concern (parent chemical and X-540) which indicated no acute or chronic risk LOC was exceeded. Excluding the X-474 degradate was considered appropriate because of the low hazard it poses, as described above.

Therefore, based on multiple lines of evidence, the Agency believes the X-474 degradate should not be included as part of the toxic residues of concern for assessing ecological risks with sulfoxaflor.

4) Section 18 Exemptions

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): The registrant first submitted sulfoxaflor for registration in 2010. Since then several section 18 exemptions have been granted for sulfoxaflor for use in Louisiana (Dec 17, 2012), Mississippi (June 1, 2012), and Tennessee (June 1, 2012) for cotton to control for tarnished plant bugs (*Lygus lineolaris*) due to resistance issues. While FIFRA's section 18 allows for pesticides undergoing registration consideration to be candidates for exemption, it is still highly irresponsible for EPA to allow unregistered, unevaluated chemicals into the environment without fully understanding and assessing risks. Time-limited tolerances for sulfoxaflor residues were not published until September 2012. At this time, EPA issued tolerances for various cotton products, the lowest of which was 0.2ppm - in or on cotton and undelinted seed.[29] Tolerances of 6.0ppm and 0.35ppm were issued for other cotton commodities. Given that honey bees do visit cotton, mostly for nectar, and the agency has since established that residues higher than 0.07 ppm will pose a risk to bees, the section 18 exemption and tolerances undoubtedly created environmental risks to honey bees that the agency did not take into account at that time. It is not apparent whether EPA conducted an ecological assessment for these Section 18 exemptions. This is clearly a regulatory failure that has plagued section 18 exemptions for many years.

Section 18 of FIFRA authorizes the agency to allow a new use of a registered pesticide or the use of a pesticide whose registration is pending (and making progress toward registration) for a limited time if the agency determines that an emergency condition exists. EPA must perform a multi-disciplinary evaluation of the request including an ecological and environmental risk assessment. The agency must deny an exemption request if the pesticide does not meet safety standards, or if emergency criteria are not met. Without strict adherence to Section 18 criteria, allowance of unregistered pesticide uses and unregistered pesticides risks an environmental and public health problem. Similar to conditional registration, allowing a pesticide like sulfoxaflor into the environmental with unknown ecological hazards is a recipe for disaster.

EPA's response:

Section 18 of FIFRA authorizes EPA to exempt State and Federal agencies from any provision of FIFRA, if EPA determines that emergency conditions exist which require an exemption. EPA can exercise this authority through the procedures in 40 CFR Part 166 to allow the emergency use of pesticides. Whether a section 18 was properly granted in the past is irrelevant to the determination of whether to grant a registration now. In 2012, EPA granted emergency exemption use under section 18 to the states of Arkansas, Louisiana, Mississippi and Tennessee to control tarnished plant bug in cotton. At the time of the authorizations, EPA had reviewed over 400 sulfoxaflor studies with the goal of ensuring public health and ecological protections and determined that the use would not cause unreasonable adverse effects on the environment. In addition, EPA reviewed the applications and supporting documentation for the section 18 requests and concurred with the governments of AR, LA, MS and TN, that emergency conditions existed for a number of growers in these states and that their cotton crops were facing significant economic loss. Thus it is not correct to state that sulfoxaflor was "unevaluated" before the emergency exemptions were issued.

EPA is unaware of any adverse incidents associated with the section 18 use in 2012. A University of Tennessee Professor of Entomology and Plant Pathology commented that he "received no reports of performance failures, secondary pest outbreaks, bee kills or other negative effects." (see #2 above, comment 0160). The Louisiana Department of Agriculture and Forestry and the Mississippi Department

[29] USEPA. 2012. Sulfoxaflor; Pesticides Tolerances for Emergency Exemptions. EPA-HQ-OPP-2012-0493; FRL-9361-4. Federal Register/Vol 77 No. 189.

of Agriculture and Commerce informed the Agency that they received no calls, heard no complaints, and were not requested to conduct any investigations.

Regarding the comment that EPA issued tolerances for sulfoxaflor residues in cotton commodities associated with the section 18 use and that these tolerances create environmental risks to bees, EPA notes that the matrices related to bees are completely different from matrices for cotton related to human consumption (e.g. through use of cotton forage for livestock). Residue trials conducted to establish tolerances for residues on fruit and vegetables, etc., follow the use pattern of the proposed label – which includes a pre-harvest interval (PHI). The PHI is the amount of time a pesticide may be applied to a crop prior to harvest. PHIs are used to ensure that residues are at or below tolerance levels by the time a commodity is distributed in commerce. The PHIs for sulfoxaflor range from 1 day to 14 days. Application of a pesticide to a crop within as little as one day of harvest would be expected to result in higher residues than what would be seen in nectar and pollen from the bloom period of that crop. Additionally, the derivation of these two residue thresholds (tolerance and bee residue in nectar) are completely different in terms of the exposure and toxicological basis and are not expected to be similar. Further, the residue in (on) a fruit may have very little relationship to that nectar. The mitigation measures taken should ensure exposure below this value for indeterminate blooming crops. The human health tolerances have no direct bearing on pollinator protection.

The FIFRA Emergency Exemption program has long supported the beekeeping industry. More section 18 authorizations have been issued to help beekeepers than have been issued to any other group. In fact, section 18 exemptions for the use of the unregistered chemical "Hop beta acids" have been authorized to help beekeepers in at least 34 states for the past 3 years. Without EPA's ability to authorize emergency use of unregistered pesticides, beekeepers themselves would be denied access to a tool to control varroatosis or to any other proposed new active ingredient that may assist in combating this pest.

5) Threats to bees and submitted pollinator study issues

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Neonicotinoids affect the nervous system of insects, causing irreversible blockage of the postsynaptic nicotinergic acetylcholine receptors (nAChRs) (via a selective agonistic mechanism).[30] Chemicals that disrupt the nAChRs - which play roles in many cognitive processes - lead to disruptions in the nervous system. In honey bees this includes disruptions in mobility, navigation, and feeding behavior.[31] Lethal and sublethal exposures have been shown to decrease foraging activity, along with olfactory learning performance and decreased hive activity.[32] Sulfoxaflor also disrupts the functioning of the nAChRs and symptoms in honey bees will be the same as seen with neonicotinoids, i.e. disruption in mobility, feeding and learning behavior.

Sulfoxaflor induces high mortality among honey bees from zero to three days post application. According to EPA's Honey Bee Risk Assessment, on average the mortality rate was as high as seven to 20 times that of controls during the first three days after application (at 3-67% of US maximum application rate). Declines in flight intensity were also observed. While recognizing the high acute toxicity of sulfoxaflor, EPA rationalizes that these effects, which include behavioral abnormalities, are "short-lived." Incredibly, it seems EPA believes that the high incidence of bee death following short-term exposure from sulfoxaflor does not factor in the long-term effects on brood and colony

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[30] USEPA. 2011. BEAD Chemical Profile for Registration Review: Clothianidin (044309). Federal Register Docket Id. No.: EPA–HQ–OPP–2011– 0865

[31] Desneaux, N. et al., 2007. Sublethal Effects of Pesticides on Benefical Anthropods. Annual Review of Entomology, 52:81-106

[32] Decourtye, A. et al., 2004. Effects of imidacloprid and deltamethrin on associative learning in honeybees under semi-field and laboratory conditions. Ecotoxicology and Environmental Safety.57: 410-419

health. However, when all or most of foraging bees are dead within three days of sulfoxaflor exposures, a long-term threat to bee colonies becomes significant, not to mention economic impacts on beekeepers who have lost the viability of hundreds of hives within a three day period.

Similarly, EPA states that "the effect of sulfoxaflor on honey bee colony strength when applied at 3-32% of the US maximum proposed rate was not apparent in most cases." However, an evaluation of effects at higher rates, but within the U.S. maximum (e.g. 75% US max. proposed rate) does not seem to be known and presents a data gap. Additionally, many of the industry studies EPA reviewed for its honey bee risk assessment contained limitations, with some results being interpreted "with caution" due to statistical weaknesses, inconsistencies with controls and design, resulting in many results being considered "inconclusive." This is especially apparent for studies examining brood development. These inadequate, "flawed" studies that lack definitive data are the basis of EPA's decision for granting registration to sulfoxaflor. Clearly, the information from these studies cannot support a sulfoxaflor registration.

Honey bee acute oral and contact LD50 values for sulfoxaflor are 0.05 and 0.13 μg a.i./bee, respectively, as determined by the agency. In many of the industry residue studies reviewed by EPA, sulfoxaflor residues in nectar were on average less than 0.07ppm. EPA states that this is the threshold value for oral and contact exposures that would not exceed levels of concern, based on the agency's calculations. Given that there is little independent data available that measures real-world sulfoxaflor residue levels, the agency does not have meaningful data to support that residues would occur less than 0.07ppm in nectar. To address this uncertainty, EPA has proposed to reduce the application rate of sulfoxaflor from the requested 0.133lbs a.i./acre to 0.09lbs a.i./acre and increase the minimum spray interval, in order to mitigate pollinator risks. EPA believes in doing so, residues in nectar would not exceed 0.07ppm. The agency also believes applications of sulfoxaflor at this 'reduced' rate would not result in brood loses or impact long-term colony health during the time period required for the conditional studies to be performed and assessed.

The agency's attempts to mitigate risks to honey bees highlight the real deficiencies in the agency's risk assessment process. Risk assessment approaches have historically underestimated real-world risks and attempts to mitigate adverse impacts with measures that prove insufficient and impractical. These risk assessment approaches make determinations that the risks are "reasonable," while failing to take into account numerous circumstances and realities that make honey bees vulnerable to chemical exposures including user failure to adhere to application rate guidelines, and local environmental conditions that may predispose crops, and other plants, to accumulate higher chemical residues, especially in nectar and pollen. In fact, EPA is just now requesting a residue study to assess the nature and magnitude on residues in a pollinator-attractive crop, further illustrating that risk estimates considered in making conclusions in this honey bee risk assessment are unreliable, and most likely will not reflect real-world scenarios, putting bees at risk. The agency must instead utilize a *precautionary approach* and wait until all the relevant data can be evaluated with respect to honey bees and other organisms before considering a sulfoxaflor registration and allowing this chemical into the environment.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369):
Although honey bee losses can be caused by a number of factors, pesticide exposure is a common theme that is both central to and integrally related to colony failures. There is no question that acute poisonings regularly kill colonies. Persistent insecticides with extended residual times applied to blooming crops continue to cause acute poisonings for pollinators for several weeks after application.

Acute kills where piles of dead bees are found are immediately obvious, but we also notice major colony declines after exposure to pesticides. Sometimes these losses appear a week after the spray event or even several months later. It is more difficult to document the precise fraction of losses that may be attributable to these sublethal effects of pesticides, but there is strong evidence of a connection. Even at the relatively low concentrations of systemic pesticides that honey bees are typically exposed to in pollen and nectar through normal foraging, research has shown that these pesticides can cause impaired reproduction and reduced queen survival (making it difficult for colonies to thrive and reproduce),[33] impaired immune function (making the bees more susceptible to pathogens),[34] disruption of hive communications (reducing the efficiency of the hive),[35] and decreased homing abilities that result in loss of foragers.[36]

The use of systemic insecticides has increased over time, as registered uses have expanded. In some parts of the country (the Midwest in particular), there is no safe place for a bee to be, with little available forage that is not contaminated with these systemic pesticides. Sulfoxaflor is a similar systemic insecticide that would further compromise the availability of clean bee forage.

The conditional registration of sulfoxaflor would add another highly acutely toxic insecticide that would be applied to blooming crops that are attractive to honey bees, like cotton, citrus and fruiting vegetables. The toxicity data clearly show that sulfoxaflor is highly acutely toxic to bees, but information on the sublethal effects is lacking. Without sufficient information on these effects that have been shown to be problematic for other systemic pesticides, US EPA should not conditionally register sulfoxaflor.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): BEAD concludes that simply waiting to spray until bees are not present will prevent losses and assumes that only acute poisonings will cause losses; however, the studies that are available in the docket suggest that sublethal exposures can adversely affect colony health over the long term. The BEAD analysis does not address the fact that sulfoxaflor will be taken up systemically by the plant and be expressed in the nectar, leading to longer-term exposure to the chemical. An assessment of the amount of pesticide to which pollinators would be exposed over time and the risk it poses to colony survival is unaddressed.

Thomas R. Smith's comment (Docket # EPA-HQ-OPP-2010-0889-0342): My evaluation of the toxicity studies leads me to conclude that the conditional registration of Sulfoxaflor will result unacceptable damage to honeybee colonies. My conclusions are based on the following:

1. The Semi Field Tunnel Study No.1 indicates the mortality of bees exposed to direct contact of Sulfoxaflor at the rate of 99 g ai/ha experienced a 7X mortality rate compared to controls. The tested 99 g ai/ha. This 7X mortality is quite close to the 10X mortality rate for Dimethoate.

2. The label recommendation for cotton of 150 g ai/ha is 33% higher than the 99 g ai/ha tested in the Semi Tunnel Study. In addition, the label will allow for two (2) treatments of 150 g ai/ha. This will expose pollinators to 133% the tested rate twice within a relative short period of time thereby compounding the effects upon the hive.

3. Residues levels exceeding 2,000 ppm in pollen and nectar were observed after two, (2),

[33] Tasei JN. 2001. Effects of insect growth regulators on honey bees and non-Apis bees. A review. *Apidologie* 32:527–546.

[34] Desneux N, Decourtye A, Delpuech J-M. 2007. The sublethal effects of pesticides on beneficial arthropods. *Annu.Rev. Entomol*. 52:81-106.

[35] Medrzycki P, Montanari R, Bortolotti L, Sabatini AG, Maini S, Porrini C. 2003. Effects of imidacloprid administered in sub-lethal doses on honey bee behaviour. Laboratory tests. *Bulletin of Insectology* 56: 59–62.

[36] Henry M, Béguin, M, Requier F *et al.* 2012. A common pesticide decreases foraging success and survival in honey bees. *Science* 336:348–350.

treatments at 0.134 lb ai/ha up to 10 days after treatment. This indicates a long period of exposure to adult bees and brood will occur at the recommended rate for cotton.

4. Studies do not indicate how these levels may affect the life span of the adult bee or the brood reared under continuous pressure of Sulfoxaflor. Studies also do not indicate how exposure affects the natural immunity to diseases and pests of the adult bee or brood raised under this condition. Recent studies have concluded that pesticide exposure has resulted in reduced honey bee fitness. The studies don't document adequately how the colony as an organism itself will be affected in its ability to communicate and achieve the necessary functions of effectively gathering pollen and nectar. Studies do not measure the ability of bees to produce royal jelly with adequate nutritional value and over the accepted period of life span to maintain the colony population dynamics. Studies do not measure the effects from Sulfoxaflor exposure to maintain hive temperatures in the short term or delayed long abilities. The colony viability can completely fail simply by its inability to precisely regulate temperature and humidity within the hive.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): A major issue with the proposed conditional registration of sulfoxaflor is that the pollinator studies submitted were incomplete and inconclusive. The current commercial neonicotinoids have been shown to have severe adverse impacts on honey bees and other non-target insects, which furthers concerns about the use of sulfoxaflor. Over the past decade, honey bee colonies nationwide have suffered record annual losses of typically about 30% to upwards of 90% in worst case situations. Pesticides have recently been identified as a primary contributing factor in these alarming population losses. Introducing yet another systemic, highly toxic insecticide to bee populations will only exacerbate these problems, contribute to the loss of beekeeper livelihoods, damage the agricultural economy, and threaten the diversity of our nation's food supply. Synergistic effects of sulfoxaflor and other stressors (additional pesticides, parasites, etc.) have also not been addressed. It is crucial to examine the realistic uses of sulfoxaflor and assess its impacts in light of the environmental stressors already faced by pollinator populations. Given the uncertainties and initial results that point to significant acute hazards, sulfoxaflor presents unreasonable adverse effects to bee species.

Studies on individual bees (Tier I) showed that sulfoxaflor is highly acutely toxic to honey bees, but further Tier II studies were incomplete or methodologically flawed. This lack of information about honey bee toxicity is an unacceptable data gap that should prevent the registration of sulfoxaflor. EPA notes several concerns with the reliability of the Tier 1 data, including:

- use of maximum residue reported in pollen and nectar to represent exposure to all bee castes and all crops
- lack of chronic toxicity data for adult and larval bees (and longer-term exposure to pupae)
- selection of the toxicity endpoint from the larval toxicity test
- accuracy of consumption rate estimates used for various bee castes
- variation in pesticide residues in pollen and nectar
- conservation of pesticide dose from plant tissue to the hive[37]

The formulated material was three times more toxic to adult bees than the technical material and the oral toxicity was even higher.[38] Measured residues of sulfoxaflor in pollen at field-application rates are three orders of magnitude (1,000-times) higher than that for imidacloprid (up to 7ppm SFX versus

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[37] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 91.

[38] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration: Appendix D, Supporting Information for Honey Bee Risk Assessment. Docket ID: EPA-HQ-OPP-2010-0889-0026.

5ppb for IMD), resulting in a high adult acute risk quotient that is unacceptable.[39] [40] Presence in pollen and nectar ensures that developing bees will be orally exposed, yet no clear evaluation of this toxicity has been done to date. Larval toxicity was slightly lower than for adults, yet real impacts on honey bee individuals and colonies under field conditions remain unknown. The chronic toxicity endpoints for adult and larval bees are missing because of limitations in the study design that precluded the use of results beyond day seven.[41] This list of uncertainties and deficiencies associated with the Tier 1 studies should be cause enough to preclude EPA from approving sulfoxaflor, but there are additional problems with the submitted semi-field studies.

EPA does not have an approved field study protocol; thus the agency has no valid field studies on which to evaluate SXF toxicity to honey bee colonies. Of the semi-field studies that were submitted, five of the six were conducted with less between 3% and 67% of the proposed maximum label rate for the US.[42] Without trials conducted at field-realistic exposure levels, EPA has no data to determine how bees, both individuals and colonies, will be affected by sulfoxaflor use. Even at the low doses that were evaluated, significant adult mortality on the day of spray application was observed, so while it is certain that higher doses will produce greater mortality, the extent of this toxicity has never been evaluated. Thus, EPA has no data on the maximal field exposure rate impacts on honey bees or any other pollinator on which to base a conditional registration. Brood and long-term colony health studies were not included or were unacceptable methodologically, compounding the unknown potential long-term chronic effects of sulfoxaflor. The long term stability and persistence of the compound indicates that chronic effects on hive populations will occur. Without information on realistic exposures, the risks associated with field usage cannot be dismissed or deemed acceptable. The evidence from the pollinator studies points to unreasonable adverse effects to honey bees, which precludes EPA from approving the conditional registration.

EPA's response:

A. Beyond Pesticides. *Sulfoxaflor results in high incident of bee death, with all or most of forager bees dead after three days. This will result in a long-term threat to bee colonies*

Agency Response. Additional information is provided here to clarify the observed mortality pattern resulting from sulfoxaflor exposure in the submitted semi-field studies. For example, the following graph shows the daily mortality pattern observed from one of the tunnel studies that evaluated the highest application rate currently proposed (0.086 lb a.i./A), the negative control, and the positive control (dimethoate). In this and other tunnel studies, bees are forced to feed on only treated crop inside the tunnel enclosures and product is applied when bees are actively foraging. Daily mortality in the sulfoxaflor treatment (red bars) spikes on the day of application and returns to control levels by day 3. Relative to control mortality, 488 additional bees died in the highest sulfoxaflor treatment, which represents 7% of the total hive strength in this treatment. Contrary to the comment, this magnitude of mortality does not represent all or the majority of forager bees present in the hive. Rather, it is considered to be well within the assimilative capacity of the hive due to the compensatory mechanisms that exist in honey bee colonies. This general pattern of short-term increases in mortality followed by a return to control mortality rates within 1-3 days was consistent across the other tunnel studies conducted with sulfoxaflor. In

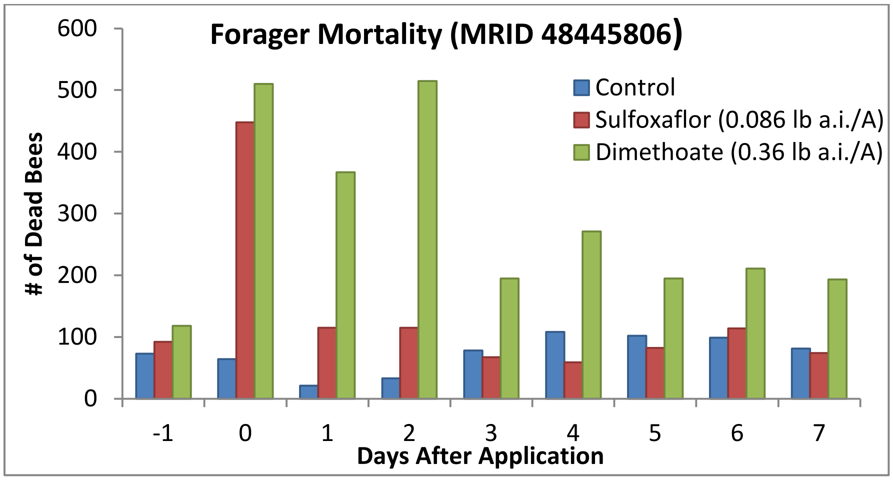
[39] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 84.

[40] Chauzat MP, et al. 2011. An assessment of honeybee colony matrices, *Apis mellifera* (Hymenoptera: Apidae) to monitor pesticide presence in continental France. *Environ Toxicol Chem.* 30(1): 103-111.

[41] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 92.

[42] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 11.

contrast, the mortality pattern observed from the reference toxicant (dimethoate) is much larger in magnitude and in duration compared to sulfoxaflor. Notably, the reference toxicant is added in order to document that the pesticide application results in exposure to bees and that adverse effects can be detected in the study.



B. Beyond Pesticides. *Information on sulfoxaflor effects at maximum application rate represents a data gap. This data gap and the limitations in tunnel studies (statistical weaknesses, control and design inconsistencies, many inconclusive results) are insufficient to support the registration of sulfoxaflor.*

Agency Response. The Agency's ecological risk assessment was based on an assumed maximum single application rate of 0.133 lb ai/A. However, this maximum allowable rate was subsequently lowered to 0.086 lb ai/A in order to reduce potential exposure to bees and other insect pollinators. At this lower rate, only 2 of the 66 measurements of sulfoxaflor residues in forager-collected nectar from the cotton semi-field study (MRID 48755606) exceeded 0.07 ppm, which is the residue value that corresponds to the acute risk level of concern (LOC=0.4) for adult forager bees (see **Figure A** below). Forager bees represent the caste of bees that is most exposed via nectar. These two values of sulfoxaflor in forager-collected nectar (0.073 and 0.127 ppm) both occurred within the first day after application and correspond to acute risk quotients of 0.4 and 0.7, respectively. These risk quotients are very close to the Agency's acute risk level of concern of 0.4. Similar to the residue findings for sulfoxaflor in nectar, results of sulfoxaflor measurements in forager-collected pollen show that all but 1 of the 66 samples are below 2.5 ppm, which is the residue value that corresponds to the acute risk LOC of 0.4 for adult nurse bees (**Figure B,** below). Nurse bees represent the caste of bees that is most exposed via pollen. Thus, 97% of the sulfoxaflor residues measured in forager-collected nectar and 98% of the residues measured in forager-collected pollen from the cotton semi-field study are below the Agency's acute risk level of concern. No exceedance of this residue-based LOC threshold in pollen occurred in the other three studies which quantified sulfoxaflor residues in pollen and nectar (MRID 48476601; 48445806; 48755601). Only one exceedance of the residue-based LOC threshold in nectar occurred in these same three studies, and this value (0.09 ppm) was very close to the residue-based threshold of 0.07 ppm.

In considering these results from the Tier 1 risk assessment for bees included in the ecological risk assessment document, it is important to recognize that conservative measures of exposure were used. Specifically, the highest recorded residues of sulfoxaflor in pollen and nectar are the bases of its Tier 1 risk assessment. Further conservatism was introduced by assuming that foragers would be exposed to a continuous dose at these maximum residue concentrations and no reduction in pesticide dose would occur based on its transport and processing over time and its storage within the hive. It is also important to note that the potential risk to other castes of bees is even lower due to their much lower consumption rates of pollen and nectar. In summary, the Tier 1 risk assessment for bees indicates that nearly all of the sulfoxaflor residues measured in pollen and nectar are below the acute risk LOC and those few measurements that exceed the LOC do so by a small margin. Given the level of conservatism associated with the acute risk LOC recently identified by the FIFRA SAP[43], the Agency considers the results of the Tier 1 risk assessment to indicate overall low acute risk to bees via consumption of contaminated pollen and nectar. It is further noted that the Tier 1 risk assessment does not incorporate any of the mitigation measures put forth on the sulfoxaflor label. These include restrictions that the product must not be applied 3 days prior to bloom, during bloom, or until petal fall for the majority of crops. For the remaining bee-attractive crops, advisory language to notify known beekeepers of scheduled application and to conduct those applications in early morning or late evening has also been added to the labels. These risk mitigation measures will further reduce exposure of bees to contaminated pollen and nectar in addition to avoiding exposure from direct contact with pesticide spray droplets. The Agency recognizes, however, that the studies supporting the Tier 1 risk assessment do not include effects from chronic exposures. This reflects a limitation in Tier 1 toxicity studies for bees that is common to all pesticides. Chronic effects are therefore included in the Tier 2 studies.

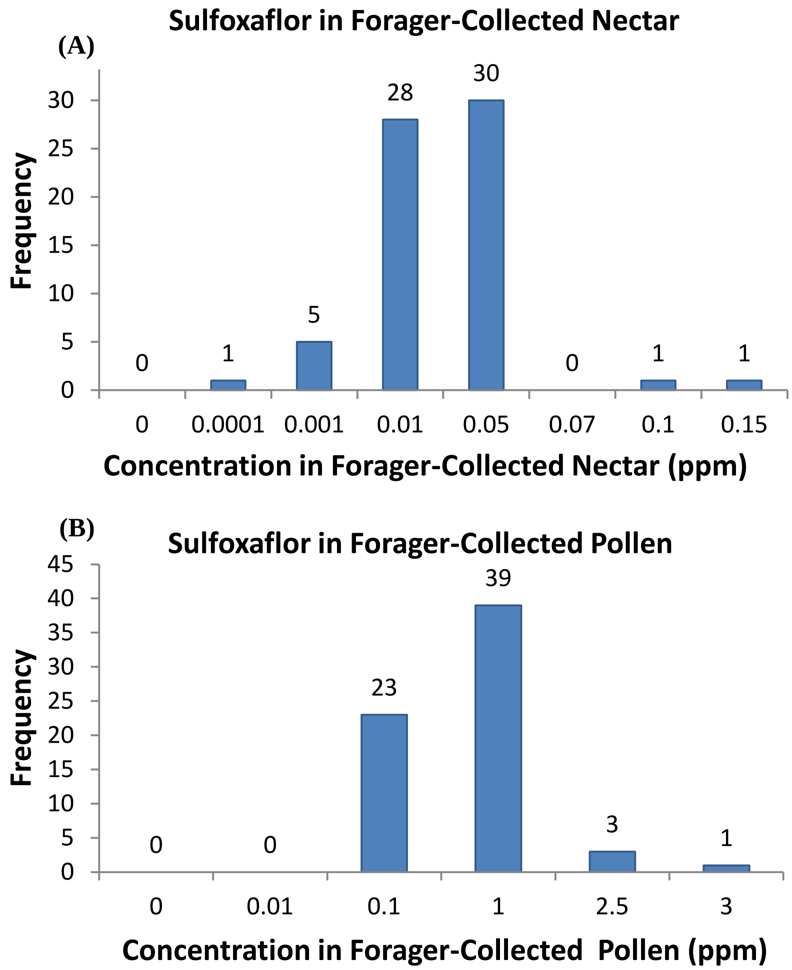
Regarding the limitations associated with the submitted Tier 2 studies in its risk assessment for sulfoxaflor, the Agency notes that these limitations were articulated in the sulfoxaflor ecological risk assessment document. Importantly, however, results from the Tier 2 semi-field (tunnel) studies represent 'worst case' exposure conditions for bees from both contact and oral exposure routes. Even with these worst case conditions, impacts on forager bee survival, flight activity and bee behavior were shown to be short lived (lasting 1-3 days). Such impacts in the natural environment are likely to be less than those observed in the semi-field tunnel studies due to bees obtaining pollen and nectar from sources other than the treated field.

Although statistical weaknesses were documented for these studies, the Agency did not rely exclusively on statistical interpretation of results in its risk findings. Rather, it relied on its best professional judgement in evaluating the magnitude and duration of effects from these studies. Therefore, the Agency believes that the statistical weaknesses did not materially compromise its interpretation of the study results. Furthermore, the statistical weaknesses noted in the sulfoxaflor Tier 2 studies are common to all semi-field studies due to practical constraints on the number of replicates that can be incorporated into the study design.

Finally, the Agency notes that the inconclusive findings from the submitted Tier 2 studies were limited to evaluation of brood development in three studies. Evaluation of brood development was considered acceptable in one tunnel study, although this was at a lower application rate (0.043 lb a.i./A). Furthermore, measures of colony strength did not demonstrate a treatment-related affect with sulfoxaflor in the Tier 2 semi-field studies. Although results from longer-term tunnel studies conducted at the current maximum single application rate of 0.086 lb a.i./A are desirable for confirming the results of the Tier 1 risk assessment, the Agency believes that when results of Tier 1 and the proposed mitigation measures are considered, the existing limitations in

[43] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0047

the Tier 2 studies do not preclude registration of sulfoxaflor given the mitigation measures (such as reduced application rates and increased minimum spray intervals) that are included on the label and the benefits provided by sulfoxaflor. Sulfoxaflor targets pests of significant of economic importance, including the tarnished plant bug threat to cotton which resulted in emergency situations in several states, as well as the Asian citrus psyllid which vectors Huanglongbing disease, the citrus greening disease, which presents an extremely serious threat to the entire Florida citrus industry. Additional pests such as the wooly apple aphid and whiteflies that have rapidly developed resistance to other insecticides will be vulnerable to the new mode of action provided by sulfoxaflor.



C. Beyond Pesticides. *The Agency has not taken into account that risk assessments historically have under estimated real world risks and that mitigation measures have proven insufficient or impractical. Further, the Agency fails to take into account numerous circumstances and realities that make honey bees vulnerable to chemical exposures including user failure to adhere to application rate guidelines, and local environmental conditions that may predispose crops, and other plants, to accumulate higher chemical residues, especially in nectar and pollen.*

Agency Response. The Agency notes that the submitted semi-field studies do take into account a number of environmental factors which may affect exposure and effects of sulfoxaflor to bees.

Such factors include temperature, humidity, precipitation, and characteristics of the treated crop and soils that all may affect exposure of bees to pesticides and subsequent effects. Furthermore, the semi-field studies confine hives and bees in tunnels during pesticide application. Therefore, they are considered to represent a reasonable ‘worst case’ exposure scenario in terms of maximizing the potential exposure of bees to pesticides via contact and oral routes. Regarding the overall nature of EPA risk assessment, the Agency believes that its ecological risk assessment process (and in particular that recently developed for bees) is appropriately conservative and reflects the current state of the science. Furthermore, risk mitigation measures such as preventing pesticide application during bloom are considered effective measures at reducing exposure and overall risk to bees from pesticide application. . For the recent Section 18 Emergency Use of sulfoxaflor on cotton, the Agency notes that no incidents involving bees (or other taxa) were reported to the Agency. The Agency notes that the commenter did not provide any evidence or examples to support their claims regarding EPA’s risk assessment process and risk mitigation measures. This prevents the Agency from responding in more detail.

D. Beyond Pesticides. *The Agency is just now requesting a residue study to assess the nature and magnitude on residues in a pollinator-attractive crop, further illustrating that risk estimates considered in making conclusions in this honey bee risk assessment are unreliable.*

Agency Response. The comment that the Agency is just now requesting a study on the nature and magnitude of sulfoxaflor residues in a pollinator-attractive crop is not accurate. Two such studies were required as part of the application for registration for sulfoxaflor (Cotton MRID 48755606 and Pumpkin MRID 48755601). Results from these two studies supported the Tier 1 risk assessment for bees. In addition, residue data were also available from two studies with *Phacelia* (MRID 48445806 & 48476601). Notably, all three crops included in these residue studies are considered pollinator attractive.

Specifically, over 600 samples of pollen, nectar, plant tissue and bees were collected and measured for sulfoxaflor among four studies and three species of plants (Cotton, Pumpkin, *Phacelia*). A breakdown of this information is provided below. OPP acknowledges that variation in residues can be expected for different crops and use patterns. To account for this variation, OPP selected the *highest* sulfoxaflor residues measured in pollen and nectar among all the available residue data as the basis of its Tier 1 risk assessment, rather than selecting an average value or a 90th percentile.

Species	**Matrix**	**No. of Samples Analyzed**	**Application Rates in lb a.i./A (No. different rates)**	**Reference**
Cotton	Plant pollen	52	0.045 – 0.134 (4)	48755606
	Forager pollen	102		
	Forager nectar	104		
	Comb pollen	83		
	Comb larvae	112		
Pumpkin	Plant pollen	24	0.022 0.089 (2)	48755601
	Plant nectar	13		
	Plant leaf	24		
	Plant nectary tissue	24		
	Plant stem	24		

Phacelia	Comb pollen	6	0.006 – 0.088(5)	48445806
	Plant flowers	6		
Phacelia	Plant pollen	15	0.021-0.043 (2)	48476601
	Plant (whole)	15		
Total Samples		**603**		

The Agency's proposed request for one additional residue study was intended as confirmatory data with respect to the findings from the residue studies for the other three crops (cotton, pumpkin and *Phacelia*). After reconsidering the overall weight of the evidence and the statutory requirements with conditional pesticide registrations, the Agency believes the existing data for sulfoxaflor are sufficient to support its registration decision in accordance with the FIFRA standard, despite some uncertainty in the currently available residue data for sulfoxaflor.

E. Beyond Pesticides. *Sulfoxaflor is a similar systemic insecticide that would further compromise the availability of clean bee forage.*

Agency Response. The Agency agrees that sulfoxaflor is a systemic insecticide; however the Agency disagrees that available information indicates its use in accordance with the proposed label will result in unacceptable adverse effects on bees for reasons stated in response to comment #5.B above. Furthermore, the available information on sulfoxaflor residues in pollen and nectar indicates it dissipates relatively rapidly, with the vast majority of pollen and nectar DT_{50} values determined to be 3 days or less. Therefore, the Agency believes that the available information indicates the proposed uses of sulfoxaflor, in combination with its specified risk mitigation measures, would not compromise the quality of forage sources to bees.

F. Beyond Pesticides. *The toxicity data clearly show that sulfoxaflor is highly acutely toxic to bees, but information on the sublethal effects is lacking. Without sufficient information on these effects that have been shown to be problematic for other systemic pesticides, US EPA should not conditionally register sulfoxaflor.*

Agency Response. As indicated in its ecological risk assessment, sulfoxaflor is classified as highly acutely toxic to bees. At the Tier 1 level, the Agency and its FIFRA Scientific Advisory Panel both recognize that existing laboratory toxicity tests with bees do not include a rigorous quantification of sublethal effects and that additional research is needed in order to identify and incorporate appropriate sublethal endpoints into standard test guidelines[44]. However, the Agency notes that the Tier 2 studies submitted for sulfoxaflor include measurement of sublethal effects (forager flight activity and abnormal behavior). In these studies, the effect of sulfoxaflor on these sublethal endpoints was limited to brief time periods after application and returned to levels comparable with controls within 3 days. The Agency also notes that the effects quantified in the submitted Tier 2 tunnel studies (e.g., colony strength) incorporate the combined impact of sublethal and lethal effects experienced by bees. Thus, while sublethal effects other than flight activity and abnormal behavior are not explicitly quantified in the Tier 2 studies, the overall impact of sublethal effects is reflected in the overall measures of colony health quantified in these studies. Therefore, the Agency believes that the Tier 1 and Tier 2 studies submitted for sulfoxaflor with respect to bees reflect the current state of the science regarding standard toxicity test guidelines for bees and are adequate to support a registration decision in accordance with the FIFRA regulatory standard.

[44] available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004 and http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0047

G. National Pollinator Defense Fund. *Persistent insecticides with extended residual times applied to blooming crops continue to cause acute poisonings for pollinators for several weeks after application.*

> **Agency Response.** The Agency notes that no specific information was provided to support this comment. Generally, however, the Agency notes that sulfoxaflor does not have an extended residual time for toxicity (foliar residual toxicity is < 3 hrs). In addition, the available information indicates sulfoxaflor residues are expected to dissipate relatively rapidly in pollen and nectar based on the vast majority of DT_{50} values determined to be 3 days or less.

H. Thomas R. Smith: *My evaluation of the toxicity studies leads me to conclude that the conditional registration of Sulfoxaflor will result unacceptable damage to honeybee colonies. Specifically:*

(1) The Semi Field Tunnel Study No.1 indicates the mortality of bees exposed to direct contact of Sulfoxaflor at the rate of 99 g ai/ha experienced a 7X mortality rate compared to controls. The tested 99 g ai/ha. This 7X mortality is quite close to the 10X mortality rate for Dimethoate.

> **Agency Response.** As addressed in the response to comment #5.A. above, the increase in forager bee mortality from exposure to sulfoxaflor is short-term in duration (< 3 days relative to controls) across all the available tunnel studies. This is in contrast to the prolonged increase in mortality observed for the dimethoate reference toxicant. The increase in mortality from the 99 g a.i./ha (0.086 lb a.i./A) represents 488 bees or 7% of the total hive strength. Given the worst case exposure conditions of this and other tunnel study, the low overall mortality rate observed with sulfoxaflor at the current maximum rate, and the risk mitigation measures put forth for most of the crops, the Agency believes that results from this study do not pose an unreasonable risk to bees.

(2*) The label recommendation for cotton of 150 g ai/ha is 33% higher than the 99 g ai/ha tested in the Semi Tunnel Study. In addition, the label will allow for two (2) treatments of 150 g ai/ha. This will expose pollinators to 133% the tested rate twice within a relative short period of time thereby compounding the effects upon the hive*.

> **Agency Response.** The maximum label rate of sulfoxaflor on cotton was reduced to 0.07 lb a.i./A. As indicated in the response to comment #5.B above, available information indicates the Agency low overall risk to bees from exposure to residues in pollen and nectar resulting from this application rate. Furthermore, the shortest reapplication interval is 5 days, for cotton; the reapplication intervals of the remaining crops have been increased and range from 7-14 days.

(3*) Residues levels exceeding 2,000 ppm in pollen and nectar were observed after two treatments at 0.134 lb ai/ha up to 10 days after treatment. This indicates a long period of exposure to adult bees and brood will occur at the recommended rate for cotton.*

> **Agency Response.** The Agency notes that on occasion, residues in pollen exceed 2 ppm (not 2000 ppm as indicated). As indicated in the response to comment #5.B above, only two of the 66 residue samples in forager collected pollen exceeded 2.5 ppm which is the acute risk LOC of 0.4 at application rates up to the current maximum of 0.086 lb a.i./A. Furthermore, available information indicates the sulfoxaflor residues are expected to dissipate relatively rapidly in pollen and nectar based on the vast majority of DT_{50} values determined to be 3 days or less at or below the current maximum application rate.

(4) *Studies do not indicate how these levels may affect the life span of the adult bee or the brood reared under continuous pressure of Sulfoxaflor in addition to other effects related to hive condition, pollen and nectar gathering, bee immune function, behavior, communication.*

Agency Response. The Agency believes that bees will not be faced with continuous pressure of sulfoxaflor due to the risk mitigation measures being implemented which avoid periods of bloom for most crops and daily time periods when bees tend to forage most actively. Additionally, retreatment intervals have been lengthened for many crops. Furthermore, available data indicates that residues are not likely to persist for long periods in pollen and nectar at levels of concern for bees. Regarding the other colony-level endpoints suggested for consideration, the Agency notes that most of these are integrated into measures of overall colony health (e.g., hive strength and brood development). Furthermore, the Tier 2 tunnel studies are designed to maximize exposure to bees from contact and oral exposure routes. The Agency notes, however, that long-term observations of colonies following sulfoxaflor application in tunnels were not available at the current maximum application rate of 0.086 lb a.i./A.

I. **Center for Food Safety.** *The current commercial neonicotinoids have been shown to have severe adverse impacts on honey bees and other non-target insects, which furthers concerns about the use of sulfoxaflor.*

Agency Response. Sulfoxaflor will have no greater impact than other insecticides currently used for pest control. It must be considered that sulfoxaflor is not classified as a neonicotinoid and as such comparison solely to neonicotinoids is inappropriate. Sulfoxaflor use will primarily displace use of existing less effective insecticides which have an activity profile which is similar to or worse than sulfoxaflor against honey bees and non-targets. These include not only neonicotinoids but also synthetic pyrethroids, organophosphates, and carbamates (carbaryl and oxamyl). As shown in UC Pest Management Guidelines for cucurbits (http://www.ipm.ucdavis.edu/PMG/r116900311.html), the generality that neonicotinoids have inherently greater adverse impact on non-targets is not correct. For honey bees alone, neonicotinoid impact is both a function of formulation and application rate. However, other insecticides have similar impacts to neonicotinoids to both honey bees and non-targets. Furthermore, use of a more effective insecticide, such as sulfoxaflor, can provide longer pest control at levels which are not conducive to economic loss economic threshold level and decrease the number of insecticide applications necessary for crop production. Fewer applications of insecticides could potentially have a positive impact on both honey bees and non-targets. Finally, the EPA agrees that the number of managed colonies in the US has declined over time, but this decline cannot be specifically linked to the registration of the neonicotinoids.
Occurrence of adverse incidents is low and include acute incidents from fugitive dust from planting of treated seed. Sulfoxaflor is not being registered as a seed treatment, and there were no incident reports from the use of sulfoxaflor on cotton for the Section 18 Emergency Use Exemption.

J. **Center for Food Safety.** *Synergistic effects of sulfoxaflor and other stressors (additional pesticides, parasites, etc.) have also not been addressed.*

Agency Response. Regarding the assessment of honey bee exposure to multiple pesticide mixtures, evaluation of pesticide environmental mixtures to any taxa is considered beyond the scope of the ecological assessment because a myriad factors can affect exposure and effects of environmental mixtures which cannot be quantified based on the available data (USEPA, 2004[45]).Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics on the exposure and effects of chemical mixtures. Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and the capabilities of the available data to allow for a quantitative evaluation of these factors. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type of interaction and factors discussed above. The pollinator assessment, however, does evaluate the risk associated with sulfoxaflor formulated products (including the inert ingredients such as surfactants that are used in formulating the active ingredient).

K. **Center for Food Safety.** *The formulated material was three times more toxic to adult bees than the technical material and the oral toxicity was even higher.*

Agency Response. The Agency's Tier 1 risk assessment for sulfoxaflor was based on the formulated product for the reasons identified in the comment.

L. Center for Food Safety. *Sulfoxaflor's presence in pollen and nectar ensures that developing bees will be orally exposed, yet no clear evaluation of this toxicity has been done to date*

Agency Response. The Agency disagrees with the commenter's assertion that it did not consider the oral route of exposure to developing bees. The Agency's risk assessment for bees considered an extensive database on the oral exposure of developing bees to sulfoxaflor, both in Tier 1 (laboratory) and Tier 2 (semi-field) studies. These studies included larval acute oral toxicity, semi-field tunnel studies, and residue studies quantifying the amount of sulfoxaflor in pollen and nectar.

M. Center for Food Safety. *The chronic toxicity endpoints for adult and larval bees are missing because of limitations in the study design that precluded the use of results beyond day seven.*

Agency Response. The lack of chronic toxicity data for adults and larvae (beyond day 7) from laboratory toxicity tests reflects the limitation in the current state of the science for bee toxicity testing. No standard protocols are available for evaluating chronic exposure to these life stages which have been validated for regulatory use. Therefore, this limitation is applicable to all chemicals, not just sulfoxaflor. Importantly, however, chronic effects on adults and larvae are evaluated using the Tier 2 semi-field studies with sulfoxaflor. Thus, in consideration of the weight of evidence concerning the magnitude and duration of sulfoxaflor residues in pollen and nectar (Tier 1) combined with the aforementioned mitigation measures and results from Tier 2, the Agency considers the available data adequate to support a registration decision in accordance with the FIFRA regulatory standard.

N. Center for Food Safety. *EPA has no data on the maximal field exposure rate impacts on honey bees or any other pollinator on which to base a conditional registration for sulfoxaflor.*

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[45] USEPA. 2004. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency: Endangered and Threatened Species Effects Determinations. Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, Washington, D.C. January 23.

Agency Response. As explained in the response to comment # 5.B., the maximum allowable rate was subsequently lowered to 0.086 lb ai/A in order to reduce potential exposure to bees and other insect pollinators. The agency has two Tier 2 tunnel studies that include this application rate and both indicate no treatment level effect on hive strength over the duration of these studies. The Agency notes, however, that long-term observations of colonies following sulfoxaflor application in tunnels were not available at the current maximum application rate of 0.086 lb a.i./A. However, given the weight of information concerning the magnitude and duration of sulfoxaflor residues in pollen and nectar combined with the aforementioned mitigation measures, the Agency considers the available data adequate to support a registration decision in accordance with the FIFRA regulatory standard. Regarding the adequacy of existing data, OPP notes that the available information on sulfoxaflor residues in bee-related matrices is actually quite extensive.

6) Bee assessment in economic analysis

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): Attempting to limit the time of application (both seasonal and time of day) with label statements is not effective for protecting honey bees for all pesticides and crops, and some inaccurate assumptions were made about bee behavior on specific crops. In particular:

Cucurbits: The assumptions that bees do not work the plants all day long is incorrect. Foraging activity and other honey bee activity near a treated field is dependent upon many factors including:

1) *Varietal differences in nectar production.* For example, Honey Dews and squash produce more nectar than other cucurbits, which the bees will forage on the entire day, until dark if temperatures permit.

2) *Hive placement.* The BEAD study states that the bees are at little risk because they are not working the plants in the afternoon. But the analysis does not assess the risk to the hives placed at the field edge and inside the field, which is common practice to accommodate the preferred stated 200 yard effective foraging habit. It is true that the greatest number of visits occur very near to hive. Those same bees, even if not foraging in the crop, are flying within the treatment area to access water or to forage on other nearby flowering weeds and plants. Blooming weeds are very problematic to growers in cucurbit fields because of the crop's sensitivity to most herbicides. Hand weeding costs can be as high as $100 per acre. Hand weeding culturally only occurs when the crop is young. Yet no risk was assigned to pollinators foraging in the blooming weeds in the field.

3) *Temperature.* The BEAD analysis states that bees stop working the crop in the afternoon. That is not true in areas of the west. The bees return to forage for nectar once the temperature drops and the plant begins to accumulate nectar in the blooms.

Night application of current pesticides is the most common recognized practice in cucurbits to reduce pollinator kills. It is not clear if this method will work to reduce kills from sulfoxaflor, since the data on sublethal effects are inadequate to make this determination. The data that do exist indicate that sulfoxaflor residues contaminate pollen and nectar for many days.

The results of a survey conducted in service to the EPA Pesticide Program Dialog Committee Pollinator Workgroup[46] indicated that cucurbits were responsible for some of the highest losses observed by beekeepers through acute poisonings (Figure 2). It is important for BEAD to get the facts correct in the interest of avoiding further losses. With the inadequate mitigations proposed

[46] PRI, 2012. *Survey on Acute Pesticide-Related Bee Kills.* Pesticide Research Institute. http://www.pesticideresearch.com/site/?page_id=24.

in the BEAD analysis, future acute kills from sulfoxaflor applications are highly likely.

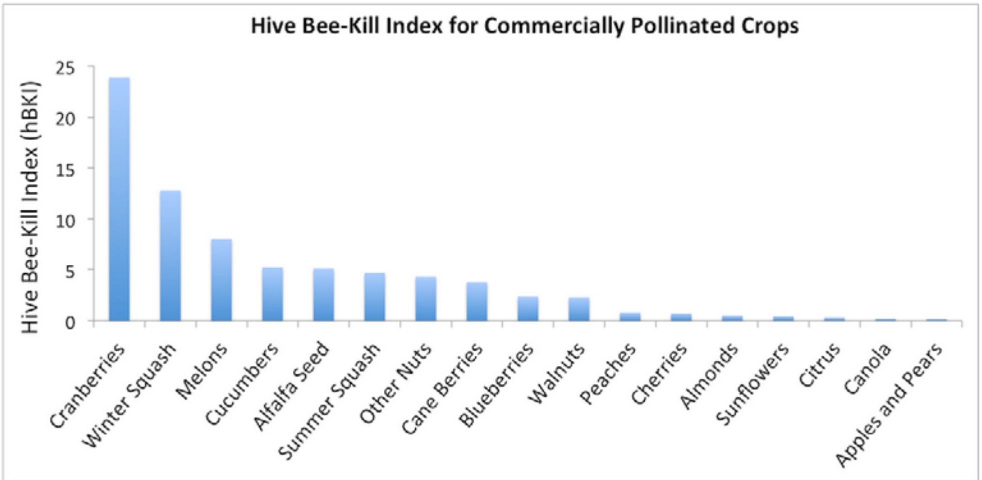


Figure 2: The hive bee-kill index is a measure of number of acute poisonings per acre of crop planted. For a detailed description of the index, see http://www.pesticideresearch.com/site/?page_id=2360/.

Cotton: The assumption that bees have only limited contact with cotton is incorrect.

1. Bees readily work cotton for nectar. This information is well documented by USDA and during the years of the Indemnity program, the cotton honey price was quoted monthly in the *American Bee Journal* and *Gleanings In Bee Culture* trade magazines up until the honey grading system changed in the late 1980's.
2. Bees are exposed to copious amounts of pollen as they enter the cotton flower to collect nectar. They return to the hive with pollen, which will remain on the body hairs. The house bees clean the worker bees of the remaining pollen on their bodies with their mouth parts. The pesticide will enter the food chain of the hive via the cleaning process that takes place inside the hive.
3. Bees do work the cotton flower and plant nectaries during late afternoon hours until dark. Bees do stop working cotton during the typical high daytime temperatures that occur in the cotton belt. However, the bees return after their afternoon Siesta and forage heavily in the late afternoons—many times and areas until dark. Late daylight afternoon applications will result in exposure to the application and the highest pesticide concentrations.
4. The effective weed control of "Roundup Ready" technology has drastically reduced blooming weeds within the field. The common use of Roundup around cotton field edges, ditches and waterways reduces the availability of forage for pollinators. This results in more intense foraging within the cotton field itself.
5. Cotton areas in which Roundup-resistant weeds have evolved present a risk from blooming weeds. Palmer Amaranth, being the most common weed to develop resistance to Roundup, is highly attractive to pollinators as a source of both nectar and pollen. These plants require pollen to be moved from the male plant to the female plant. A pollinator must do that. Fields with these Roundup-resistant blooming weeds will be VERY problematic for pollinators unless near 100% weed control is achieved. If achieved, the risk returns to the number 4 scenario.

A major flaw in the BEAD risk assessment is that it assumes that if pollination is not beneficial to the plant, the risk is low. It does not assess the risk from use of the plant by pollinators. This is clearly stated in cotton. For citrus, the assessment takes into account the use of the citrus flower by the pollinator. The practice of only allowing pesticide applications to citrus during periods of no bloom should protect pollinators if no blooming weeds are present in the field and if sulfoxaflor is not persistent in plant tissue. However, EPA has no data that would demonstrate that either of these conditions holds true. The conditional registration of sulfoxaflor would result in managed honey bee colonies becoming the unwitting test subjects, and the beekeepers who own them would be made to pay the price if sulfoxaflor proves to be highly toxic on a sublethal basis as well.

Thomas R. Smith's comment (Docket # EPA-HQ-OPP-2010-0889-0342): The economic assessment published by EPA is unacceptable from the standpoint of establishing the benefit of managed honeybees. The assessment myopically assesses the pollinator worth solely based of the pollination benefit to the individual treated crop. The colonies exposed in the cotton field are the same colonies which will be exposed in all the other pollinated dependent crops. The assessment lacks the understanding of the relationship between managed honeybees and production agriculture. Managed honeybee colonies are moved thought the nation to meet the demands of crops requiring pollination. This fact will result in multiple exposures where crops in bloom, which has not been acknowledged nor the potential economic damage properly assessed. If a colony is damaged due to exposure on cotton to the level where it cannot be utilized to commercially pollinate crops, those crops are at risk of an inadequate supply of available pollinators and/or the additional costs of supply and demand. Simply put, it externalizes the costs onto other persons, the beekeeper and the farmer of pollination dependent crops. The growing need for pollinators in the United States is clearly establish by the RaboBank report on pollinators and should be carefully reviewed.

The economic assessment description of how honey bees are managed during the commercial pollination of crops indicates complete lack of knowledge of the actual physical and biological facts. It describes field conditions and plant physiology which are not representative. For example: Colonies are commonly placed within the field borders of most fields in order to achieve maximum pollination. The assessment states colonies are placed on field border giving justice to the recommendation for "late afternoon" application. (Whatever "late afternoon" actually is) The assessment states that nectar production ceases around mid-day in melon fields. This is incorrect and, when in fact, nectar production is dependent upon many variables including varietal type, cultural practice, weather conditions, soils and, location. In my experience, melon plants cease producing nectar during mid-day heat and begin to produce nectar again as temperatures cool later during afternoon. Bees begin to forage the flowers for nectar in the late afternoon until dark if temperature permit. Colonies can utilize the field for collection of water throughout the day. Weeds are always problematic to melon fields because of their sensitivity to herbicides. Blooming weeds are present almost without exception in melon fields. Pollinators will forage blooming weeds for pollen and nectar throughout the day until light fades or temperatures prohibit foraging. The colonies located within the field are vulnerable to exposure as the fly to forage or collect water.

I describe these short comings in the assessment to point out the fact that the assessment is focused on avoiding the obvious risk mitigation measure, which is to APPLY AFTER DARK. The assessment is unaware, based on its discussion, that SPRAYING AFTER DARK IS THE MOST ACCEPTED AND OBSERVED CUTURAL PRACTICE FOR PROTECTING POLLINATORS WHEN COMMERCIALY POLLINATING CROPS.

Several assumptions made about cotton and bees are incorrect. The assessment states that bees do not readily enter the cotton flower to collect pollen or nectar. Also stated is that cotton pollination can be improved by 3-30% based on studies. My point is: How can pollination be improved if bees do not readily enter the flower? I observe bees readily entering open cotton flowers to collect nectar. These nectaries are located at the base of the flower where the highest viability pollen also occurs. This requires the bee to press itself between the anthers and the pedals to gain access to the nectar. When the bee exits the flower, the bee is covered with copious amounts of pollen on its body. Pictures were provided to Environmental Fate and Effects Division in 2012. The bee returns to the hive where the house bees clean the remaining pollen off the forager with their mouth parts thus providing the entry point to the hive food chain. The assessment states that bees do not work cotton for nectar or pollen in the afternoon. That is completely false for the western U. S. Bees readily reenter the cotton field in late afternoon until dark to gather nectar. Bees enter the cotton fields at first light and forage until about mid-day. As in the case for melons, the assessment goes to great extent to justify spraying in the "late afternoon" as opposed to at night when the bees are certain not to be present and exposed to direct contact or the highest toxicity levels.

Toxic levels of Sulfoxaflor on cotton will most certainly result in a great threat all pollinator due to its attractiveness to pollinators. Cotton produces much nectar and bees will fly up to 2 miles to gain access to that nectar source. The Cotton Council has promoted studies as factual stating bees don't prefer to forage on cotton "very much". Historically cotton is one of the top two problematic crops for pesticide related damage to pollinators, along with citrus. A price for cotton honey was quoted monthly in the American Bee Journal and Bee Culture trade magazines in the 1970's and 1980's. A California price and a Southern US price were quoted for cotton honey. In the 1990's the U.S. honey pricing changed from a floral/color source system to a standardized color grade system. Original copies of these trade magazines for reference.

The assessment states that applications on citrus would be best when no bloom was present because of its attractiveness to honeybees. The glaring admission of this statement is that bees are at great risk when they are "visiting", or "actively visiting" any plant in bloom. If the risk exists for citrus, the risk exists for all blooming crops. Pollinators must not be deemed expendable in one crop and not the other. They are either expendable or not expendable. NOT EXPENDABLE!

EPA's response:

The EPA's impact assessment was only intended to evaluate the potential role that sulfoxaflor may play in production of the various crops for which registration is being sought and to provide supplemental information regarding the importance of honey bees for production of these crops. BEAD's role in the assessment process is to examine whether the new pesticide meets a need that is not being met by currently registered pesticides or non-chemical alternatives and determines if the benefits from the new pesticide are greater than those from currently registered pesticides or non-chemical pest control measures. As such, BEAD only assesses the benefits of registration.

EPA agrees with the commenters that foraging activity and other honey bee activity near a treated field is dependent upon many factors. These factors will vary according to crop, variety, meteorological conditions, hive placement, etc., and therefore it is not plausible to evaluate all potential bee activity for all situations. When commercial beekeepers place hives in the field borders or directly in fields (as noted in the comments), protection of the hives is best established through the formal agreement of responsibilities between the bee keeper and the farmer. This agreement should include water availability, weed management, and other factors which the parties determine are relevant to the individual situation. It must also be pointed out, that not all weeds are attractive to honey bees. It is implausible to evaluate every weed which may be encountered in the assessed crops as their attractiveness to honey bees may vary both spatially and temporally and as a function of weed diversity in a given area. EPA does note that, in contrast to the comments regarding honey bee activity in melons until dark, collection of pollen usually ends before noon and nectar collection may continue into late afternoon (Mussen and Thorpe, University of California, publication 7224).

EPA acknowledges that honey bees do enter cotton fields. The impact assessment provides information relative to the importance of honey bees to cotton production. Based solely on the reproductive biology of cotton, EPA concluded that honey bee pollination can increase yields but is not essential for cotton production. EPA has seen no data which would indicate that use of sulfoxaflor would result in a greater detrimental impact on honey bees than the currently registered alternative insecticides. EPA also believes the additional labeling mitigation will reduce exposure to bees and therefore the potential for downstream effects would be minimized. Furthermore, availability of sulfoxaflor as an efficacious alternative insecticide could potentially reduce the impact on honey bees through a reduction in overall number of insecticide applications when based on the economic threshold component of IPM programs.

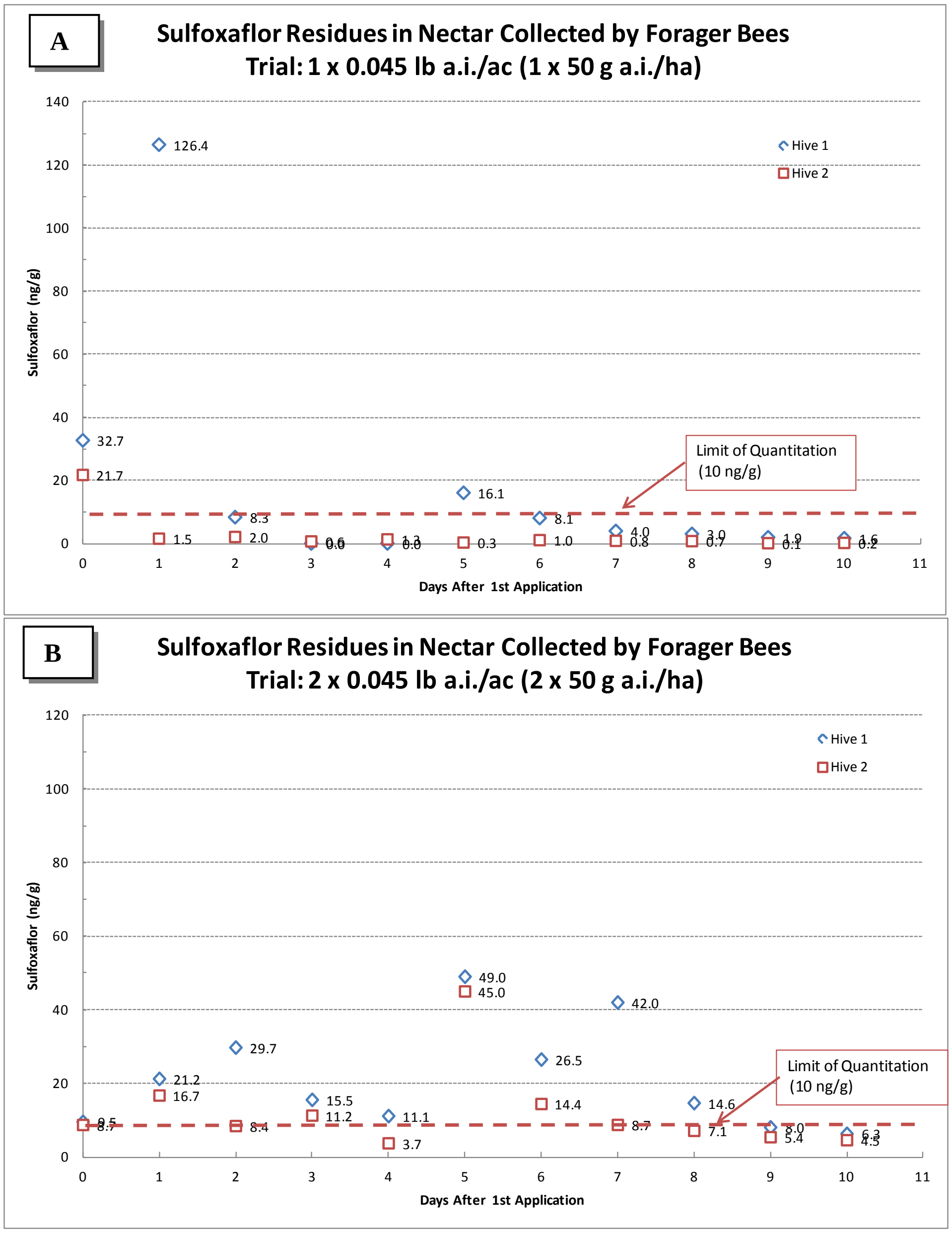
A recent review by EPA of a Section 18 Emergency Exemption for the use of sulfoxaflor on cotton, indicates that some farms in mid-south cotton production are currently applying up to 16 insecticide applications to control the tarnished plant bug. These insecticide applications include organophosphate, pyrethroids, and neonicotinoids, all of which are capable of honey bee mortality. The increase in number of applications over previous years is largely a result of increased insecticide resistance and lack of efficacy of currently registered insecticides. In order to control tarnished plant bug, producers have been forced to apply insecticides in combination cocktails, which in turn further limits insecticide availability for complete season control of the pest. Furthermore, application of many of these insecticides results in outbreaks of secondary pests which in turn must be controlled by insecticide application. Data reviewed by EPA indicates that sulfoxaflor provides superior efficacy to most of the currently registered alternatives for key pests in cotton production. The use of sulfoxaflor would result in fewer pesticide applications overall (see commenter #s 0062, 0308, and 0059).

EPA agrees that effective weed control could be assumed to increase bee foraging directly on cotton. However, EPA has seen no data, nor did the commenter provided data other than anecdotal, which would either confirm or dispel this assumption. EPA is aware that Palmer amaranth has developed resistance to Roundup. However, EPA believes that a substantial stand of Palmer amaranth in a cotton field would trigger additional weed control measures by the farmer to ensure maximum yield and to prevent the weed from spreading to a wider area or greater density. Typically, farmers aim to control Palmer amaranth in the vegetative stage before flowering which would preclude its use by pollinators. In fields with high Palmer amaranth populations, farmers will often mow their fields to prevent the spread of this weed.

BEAD did note that cucurbits are one of the most dependent crops for honey bee pollination. This does seemingly concur with the comments identifying cucurbits as being responsible for some of the highest losses observed by beekeepers through acute poisonings cucurbits. Based on the Agency's Ecological Incident Information System (EIIS), no incidents have been reported for bees and cucurbits. Based on available information and the need to provide effective pest control in these crops, EPA has no basis to determine that the registration of sulfoxaflor would increase the number of acute poisonings over that of currently registered insecticides. Rather, as sulfoxaflor has greater efficacy than many of the currently registered insecticides, it is more likely that sulfoxaflor will be used in place of numerous applications of less effective insecticides and could reduce overall honey bee insecticide exposure.

EPA did not indicate that late evening sulfoxaflor would eliminate honey bee exposure but only indicated that "honey bee exposure to sulfoxaflor can be greatly reduced by limiting applications to late afternoon". While night time applications of sulfoxaflor may provide the greatest safety to honey bees in unique situations, this application timing is not realistic across all crops and regions. Due to regional differences in topography and infrastructure, night time application could potentially jeopardize worker safety, whether ground or aerial application. However, for those unique situations where insecticide applications can be safely applied at night (e.g. application by tractor with lights), this would still be an option based on best professional judgement.

Regarding the persistence of sulfoxaflor in plant tissue, available data from the cotton residue study indicate that residues in cotton nectar tend to decline steadily to levels approaching analytical detection limits within 3-4 days following application (see Figure 1A-1D below). Nectar is considered the dominant exposure route for forager bees based on their high nectar estimated consumption relative to pollen. The one exception occurred with the highest proposed application rate evaluated (2 x 0.134 lb ai/A; Figure 1D), in which one sample with 1 ppm sulfoxaflor occurred on day 8 (3 days following the second application). The Agency notes that the maximum proposed rate of sulfoxaflor (2 x 0.134 lb ai/A) was reduced to (0.086 lb ai/A) in an effort to reduce exposure to bees. It is further noted in the ecological risk assessment for sulfoxaflor that foliar dissipation half lives are generally 10 days or less and approximately half are 3 days or less.



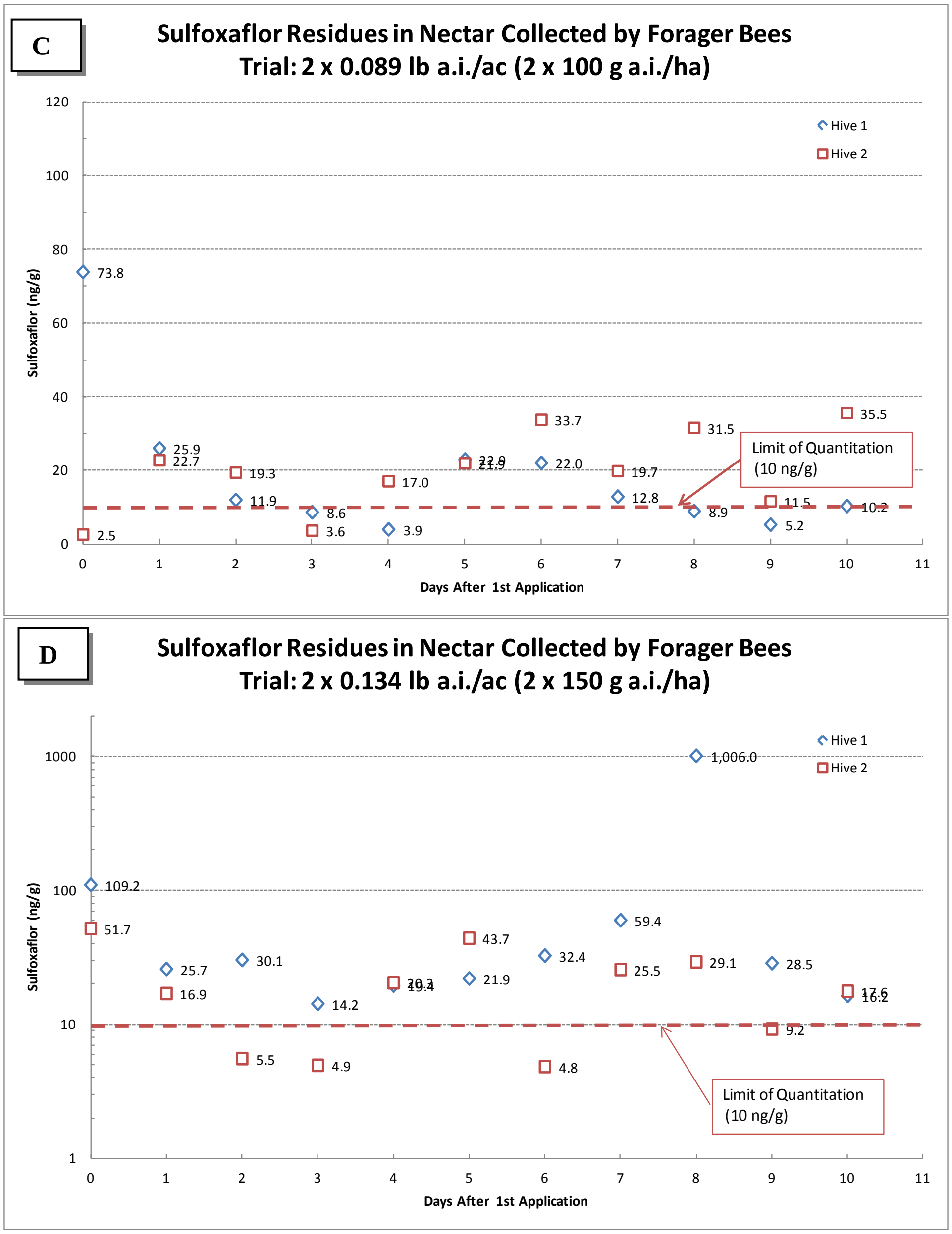


Figure 1. Profile of sulfoxaflor residues in cotton nectar following applications on Day 0 (A-D) and 5 (B-D); MRID 48755606

Regarding the assessment of honey bee exposure to multiple pesticide mixtures, evaluation of pesticide environmental mixtures to any taxa is considered beyond the scope of the EFED assessment because a myriad factors can affect exposure and effects of environmental mixtures which cannot be quantified based on the available data (USEPA, 2004). Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics on the exposure and effects of chemical mixtures. Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and the capabilities of the available data to allow for a quantitative evaluation of these factors. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type of interaction and factors discussed above. The pollinator assessment, however, does evaluate the risk associated with sulfoxaflor formulated products (including the inert ingredients such as surfactants that are used in formulating the active ingredient).

7) Impacts on commercial beekeepers

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Commercial beekeepers from across the U.S. have been reporting honey bee kills that coincide with the planting of neonicotinoid-treated corn. Beekeepers, Beyond Pesticides, the Center for Food Safety, Pesticide Action Network, and others have already voiced concern to the agency over its continued lack of definitive action on the prevalence of bee-toxic pesticides in the environment. To that end, a petition requesting the agency to suspend the neonicotinoid, clothianidin, was submitted to the agency in 2012 and was supported by over one million signatures. Commercial beekeeping adds between $15 and $20 billion in economic value to agriculture each year. Without the yield increases made possible by commercial pollination services, food prices would rise, our farm sector would become less competitive globally, and the security and variety of our food supply would diminish.

Beekeepers across the U.S. are still losing hundreds of thousands of hives, and this is only expected to continue with spring plantings. The agency has not considered the synergistic impacts honey bees may experience with aggregate exposures to neonicotinoids and sulfoxaflor. Beekeepers have routinely identified multiple chemicals in their hives, most of which were encountered by their bees foraging on treated crops. Given that both sulfoxaflor and neonicotinoids share a similar mode of action, with sulfoxaflor being more potent in toxicity, would honey bees experience an enhanced, additive toxicological response? Would sub-lethal and chronic impacts to honey bee be more devastating? Even though sulfoxaflor is not currently registered for corn, it is to be used on other bee-attractive crops that are also currently treated with neonicotinoids. Would honey bee losses increase when using both neonicotinoids and sulfoxaflor? These questions have not been considered by the agency, but are being asked by concerned beekeepers.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): The risk assessment also fails to take into account the impacts on the livelihoods of beekeepers, the national agricultural economy, and localized rural economies. Honey bees are the most economically valuable pollinator worldwide, and many high-value crops such as almonds and broccoli are entirely reliant upon pollination services by commercial beekeepers. Of the 100 crops that provide 90 percent of the world's food, over 70 are pollinated by bees. The value of crops pollinated by bees in the U.S. alone was estimated at $19.2 billion in 2010 – that figure has since grown.[47] This clearly multiplies the economic impacts of past EPA decisions on conditional registrations that have taken a major toll on beekeeper livelihoods, and counsels strongly against any more conditional registrations for additional neonicotinoids such as sulfoxaflor.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): Consideration of the livelihood of the many small business owners who are commercial beekeepers is only a part of the economic analysis. In fact, according to the USDA, the pollination services provided by our bees are worth $15 billion in crop value in the U.S. alone.

EPA's response:

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[47] Calderone NW. 2012. Insect Pollinated Crops, Insect Pollinators and US Agriculture: Trend Analysis of Aggregate Data for the Period 1992–2009. *PLoS ONE* 7(5): e37235.

The impact assessment was developed to evaluate benefits which would be associated with the registration of sulfoxaflor. Economics were not a component of this impact assessment. EPA appreciates the concerns expressed as to potential impact on beekeepers and the overall agricultural economy. EPA believes the additional labeling mitigation will reduce exposure to bees and therefore the potential for downstream effects would be minimized. Further, EPA would like to point out that while the commenters believe that there is a cascade effect for migratory beekeepers and pollinator dependent crops, there is also an impact on crops which do not rely on pollinators. While it is important to protect the pollinators to ensure the economic viability of pollinator dependent crops and commercial beekeeping, it is likewise important to ensure the economic viability of non-pollinator dependent crops by ensuring the availability of pesticidal tools to control pests which cause serious economic impact. The proposed label language as well as continued collaboration between beekeepers and growers, both by formal agreement and as common courtesy, should provide a balance and provide economic benefits to both.

Growers believe that without obtaining use of a chemical with a new mode of action such as sulfoxaflor, they may experience significant economic impacts and failure of their IPM programs. They state they would be forced to continue to rely on older chemistries, of which most pose risk to bees. Many growers familiar with field trials of sulfoxaflor said it is more effective on specific target pests and less injurious to beneficials. The use of sulfoxaflor can reduce the potential adverse effects from multiple applications of other pesticides. An IPM specialist from UC Riverside reported that registration of sulfoxaflor will reduce the number of applications of chlorpyrifos used to control citricola scale infesting citrus (comment 0161). If bees are foraging in or near citrus, this will lower their exposure to this organophosphate. Furthermore, a commenter from Louisiana State University AgCenter stated that the insecticides used for managing plant bugs in cotton rely heavily on organophosphates and neonicotinoids (see #2 above, comment 0059). He wrote that due to resistance issues they have seen a shift to the OP, acephate, synergized with pyrethroids, and neonicotinoid/pyrethroid mixtures. The commenter noted that unfortunately these insecticides have detrimental effects on arthropod natural enemies leading to outbreaks of secondary pests. Acephate is notorious for flaring spider mites, and pyrethroids are notorious for flaring spider mites and aphids. Thus, follow up applications of miticides or aphicides are often necessary following insecticide applications targeting plant bugs. Reducing the number of applications of insecticides would lessen the exposure of bees to these products.

The Agency conducted an extensive analysis of sulfoxaflor, encompassing all aspects of the pesticide, and focusing exhaustively on the pesticide's potential effects on animals, plants, soil, and water. EPA believes its analysis with respect to sulfoxaflor was consistent with the requirements of FIFRA.

Regarding the assessment of honey bee exposure to multiple pesticide mixtures, evaluation of pesticide environmental mixtures is considered beyond the scope of the ecological assessment for any taxa because a myriad factors can affect exposure and effects of environmental mixtures which cannot be quantified based on the available data (USEPA, 2004[48]).Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics on the exposure and effects of chemical mixtures. Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and the capabilities of the available data to allow for a quantitative evaluation of these factors. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type of interaction and factors discussed above. The pollinator assessment, however, does evaluate the risk associated with sulfoxaflor formulated products (including

[48] USEPA. 2004. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency: Endangered and Threatened Species Effects Determinations. Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, Washington, D.C. January 23.

the inert ingredients such as surfactants that are used in formulating the active ingredient).

8) Commercial beekeeping as a migratory operation

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): The largest single fact that BEAD did not account for is that the bees that may be exposed to sulfoxaflor in cotton, tomato, citrus and cucurbit fields are the same bees that are absolutely critical for pollinating almonds, cherries, apples, pears, cranberries, blueberries, and more. It is almond pollination season right now, and there is a serious shortage of hives to fill the need for pollination services. The killing of bees by sulfoxaflor applications to cotton, cucurbits, and other fruits and vegetables may not affect the value of those crops, but it will affect both the livelihood of commercial beekeepers and the pollination services we provide to many other high-value crops. As the RaboBank report describes, the loss of commercial pollination services would result in substantial economic losses to agriculture as a whole.

EPA's response:

EPA acknowledges that bees may potentially be exposed to sulfoxaflor in numerous crops. However, EPA also acknowledges that sulfoxaflor is but one of many insecticides to which bees would potentially be exposed across the complex of crops mentioned in the comments. Exposure to multiple insecticides and/or multiple exposures to a single insecticide is inherent for mobile bee populations as hives are relocated throughout the country. Furthermore, and most importantly, EPA must point out that use of the other insecticides also has the potential for bee mortality. EPA is not aware of any information that would indicate that honey bee losses as a result of exposure to sulfoxaflor would exceed or be any different than those currently experienced with currently registered insecticides. EPA also believes the additional labeling mitigation will reduce exposure to bees and therefore the potential for downstream effects would be minimized. Furthermore, reliance on the most effective insecticides, such as sulfoxaflor, has the potential to increase levels of pest control and ultimately serve to reduce overall number of insecticide applications, as dictated by economic threshold levels of IPM programs, and therefore honey bee exposure.

Whether sulfoxaflor is or is not used on different crops, commercial honey bees will be exposed to a diverse array of pesticides and possibly other toxicants while they are transported around the country. Risk characterization integrates exposure and effects to provide an estimate of risk. Whether bees are managed as "for-hire" migratory colonies or are raised in stationary hives, they cannot be confined. A determination of quantifiable exposure from all sources to "free-roaming" organisms is extremely difficult.

9) Bee incident reporting system

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): On a related note, EPA does not have an effective system in place for beekeepers to report bee incidents or have claims investigated. While much of the investigative actions belongs to states, beekeepers are frustrated that the federal agency has not played a major role in investigating incidents. Beekeepers believe that sulfoxaflor will compound their problems with bee losses, and find the agency irresponsible for proposing the registration of another chemical toxic to bees before sufficiently addressing the issues surrounding already registered chemicals that have an undeniable link to current bee losses. To that end, EPA must carefully consider the impact that registering sulfoxaflor would have on the livelihoods of commercial beekeepers.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): The proposed use of the conditional registration process begs the question of how EPA will determine whether sulfoxaflor can safely be used in agriculture. At present, there is no viable system for reporting and tracking pesticide poisonings of honey bees when they occur, making it impossible to document kills caused by problematic pesticides and restrict their use. It is critical that EPA develop and implement a valid mechanism for tracking poisoning events prior to the registration of sulfoxaflor and use this system to gather data on potential adverse effects.

EPA's response:

EPA receives incident data and it can be informative. EPA has a viable incident reporting system with a dedicated phone number and dedicated staff in attendance. The contact information has been published in bee journals and is listed on EPA's website. Historically, commercial beekeepers in particular have shown great reluctance to report incidents. State Lead Agencies and EPA have been told that beekeepers do not wish to offend growers who either hire their pollination services, or allow them on their land. However, EPA has reached out continuously, both on an individual basis, and publicly (such as at the 2013 North American Beekeeping Conference) to urge beekeepers to report incidents. Under FIFRA section 6(a)(2), pesticide registrants must submit factual information regarding unreasonable adverse effects on the environment. For example, Bayer submitted an incident report on the 2008 beekill incident in Germany and an independent investigation by Bayer of two beekill incidents in the Midwest in 2012. Both provided useful information on residues (or lack thereof) that were later corroborated by the state lead agencies. Further, Syngenta has provided incident reports where adverse effects have been detected in on-going studies underway in the European Union. These reports have alerted EPA to effects well before the study was completed and are used to inform risk assessments.

EPA has received no reports on any sulfoxaflor-related incidents from the 2012 use under section 18 authorizations. The state lead agencies informed EPA that they were not asked to conduct any investigations and they received no reports of adverse incidents.

10) Concern for birds

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Sulfoxaflor raises concerns for bird populations as well. In a major scientific assessment that will soon be released by American Bird Conservancy, toxicologist Pierre Mineau reviews the effects of neonicotinoid insecticides on avian species and the aquatic systems on which they depend. The report raises red flags for birds that may apply to sulfoxaflor as well. EPA needs to proceed with caution.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): The environmental persistence of the sulfoxaflor degradates and their neonicotinoid-like mode of action raise health and environmental concerns that go well beyond invertebrates. EPA identifies slight acute toxicity risks to birds, but states that sulfoxaflor is "practically nontoxic" on a sub-acute dietary basis. However, the passerine study on zebra finches was incomplete, and the acute oral LD50 could not be determined.[49] This is an area of uncertainty in the avian acute risk estimation that should be addressed with a second study.[50] Data is also lacking on effects from consumption of contaminated drinking water for all species, and EPA says that "sulfoxaflor exposure through drinking water alone has the

[49] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 68.
[50] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 90.

potential to be a relevant acute or chronic exposure route of concern for mammals or birds."[51] EPA also says that "additional refinements are needed to determine if actual risks result from this [drinking water] exposure pathway," but these refinements were not conducted.[52] This clearly shows a route of exposure and area of concern that is not adequately assessed by the EPA's RA that poses significant detrimental impacts to non-target species. In the case of imidacloprid, numerous recent studies have indicated surface water contamination exceeding EPA–recognized safe levels. The persistence of sulfoxaflor's metabolites in aquatic environments raises concerns similar to those posed by imidacloprid and other neonicotinoids. There are a number of concerns about the effects of neonicotinoids on avian species and the aquatic systems on which they depend that are only now being explored, and sulfoxaflor may pose similar threats.[53] Sulfoxaflor should not be approved without complete acute, subacute, and reproductive toxicity information on avian species, including completion of the passerine study.

EPA's response:

The lack of an LD_{50} in the avian passerine study with zebra finch occurred because birds regurgitated the dose at higher concentrations. Therefore, this study was unable to determine the extent to which birds that displayed this regurgitation behavior were exposed to sulfoxaflor. Passerine species tend to be much more prone to regurgitation of oral doses compared to Galliformes (quail) and Anseriformes (mallard duck). To account for this uncertainty, EPA made a conservative assumption in calculating its risk quotients (RQ) by using the highest tested dose which did not result in significant regurgitation as the denominator (80 mg/kg bw). The actual LD_{50} is expected to be greater than 80 mg/kg bw because no mortality occurred at this dose. Because the acute RQ for small (20g) birds consuming short grass is 0.70 based on the highest predicted EEC, only a slight increase in the LD_{50} (to approximately 100 mg/kg bw) would result in an acute RQ below the non-listed species LOC (0.5). Risk quotients for all other dietary items are all below the acute risk to non-listed species LOC of 0.5. Furthermore, it is apparent that the dietary concentration associated with an acute RQ of 0.5 (38 ppm on short grass) is exceeded for only 6 days out of the year based on T-REX modeling. Therefore, given conservative assumptions used in the passerine risk assessment and the likelihood that an additional study would lead to a finding of lower risk (not greater risk), the need for an additional study was not considered necessary.

Regarding the screening level assessment for drinking water exposure to wildlife using the SIP model, it should be understood that this assessment is only able to eliminate drinking water exposure as a potential exposure route of concern for concern and is not intended for identifying whether drinking water is actually a risk concern Specifically, the SIP model relies on highly conservative (upper bound) exposure assumptions including: 1) the concentration in the bird and mammal's drinking water is equivalent to the chemical's limit of solubility in water, and 2) 100% of the drinking water consumed by birds and mammals is contaminated at this level. Therefore, if based on these highly conservative estimates, the upper bound estimate of drinking water exposure is below the acute and chronic levels of concern, then it is concluded that that exposure through drinking water is not a concern. However, if the upper bound estimate of drinking water exposure exceed the levels of concern, then additional refinements are necessary in order to conclude whether there actually is a risk concern. For sulfoxaflor, if one assumes exposure via drinking water exposure pathway based on the aforementioned conservative assumptions, EPA cannot conclusively discount drinking water as a potentially relevant exposure pathway. This, however, does not indicate that drinking water is a risk concern. Additional refinements of the wildlife

[51] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 109.

[52] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 20.

[53] See forthcoming report from the American Bird Conservancy and toxicologist Pierre Mineau for more details.

drinking water exposure assessment are required before risk conclusions can be made. Currently, EPA does not have approved models for refining risk estimates to wildlife via drinking water. However, such approaches are in development and should be available for refining such screening level assessments in the future.

11) Concern for aquatic ecosystems

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): Aquatic ecosystems and the species that depend on them also face risks from systemic pesticides including sulfoxaflor. Surface water contamination resulting from the use of sulfoxaflor is expected to occur mainly from drift, rather than run-off. Plant residues that are left after crops are harvested are another potential route for surface water contamination. Drifted sulfoxaflor that reaches aquatic systems will likely persist, while that reaching soil systems is expected to break down quickly.[54] However, this assumption does not account for the major soil degradate, X-474, which is mobile and can run-off following sulfoxaflor application into surface waters. EPA states that "both surface and ground water contamination is expected from these three degradates following leaching drift/run-off events," clearly identifying a potential route of exposure for aquatic systems.[55] The RA does not assess the impact of the major degradate X-474 on aquatic environments, which should be remedied before sulfoxaflor is considered for registration.

While the acute toxicity to most aquatic species (flora and fauna) was determined to be fairly low, sulfoxaflor is highly acutely toxic to saltwater invertebrates.[56] This poses concerns for coastal uses of sulfoxaflor, but there is no apparent proposed mitigation through labeling or otherwise. Without mitigation and further exploration of sulfoxaflor's, and its degradates', toxicity to saltwater invertebrates, the use of sulfoxaflor in coastal areas presents a serious threat to estuarine and marine ecosystems.

Chronic toxicity of sulfoxaflor to aquatic species is examined, but the possibility for contamination of surface waters above the levels of concern is not addressed. In a key recent paper, Starner and Goh (2012) document that a significant portion of sampled surface waters were contaminated with imidacloprid above EPA-allowed levels for chronic invertebrate exposure across diverse agricultural landscapes in California.[57] Several other studies by the U.S. Geological Survey have found comparable aquatic contamination from the systemic neonicotinoids, which are similar in action to sulfoxaflor, in other environmental contexts.[58] The aquatic persistence of sulfoxaflor and its degradates, especially in anaerobic conditions, suggests that there may be similar levels of sulfoxaflor detected in waterways should it be registered. However, the proposed RA framework does not mention these water contamination studies nor does it quantify the risks to other species from comparable sulfoxaflor water contamination. The fact this environmental contamination by a major neonicotinoid exists now in California and elsewhere is indicative of agency failure to prevent undue consequences in its past risk assessments. The sulfoxaflor RA must be revised to correct this omission, or similar water contamination from sulfoxaflor is likely to impact aquatic ecosystems.

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[54] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 10.

[55] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 10.

[56] EPA. Environmental Fate and Ecological Risk Assessment for Sulfoxaflor Registration. Page 10.

[57] Starner K and Goh KS. 2012. Detections of the Neonicotinoid Insecticide Imidacloprid in Surface Waters of Three Agricultural Regions in California, USA, 2010-2011. *Bull Environ Contam Toxicol.* 88(3):316-21.

[58] Hladik ML and Calhoun DL. 2012. Analysis of the Herbicide Diuron, Three Diuron Degradates, and Six Neonicotinoid Insecticides in Water – Method Details and Application to Two Georgia Streams. USGS Scientific Investigations Report 2012-5206.; Smith KP. 2011. Surface-Water, Water-Quality, and Meteorological Data for the Cambridge, Massachusetts, Drinking-Water Source Area, Water Years 2007-08. USGS Open-File Report 2011-1077.

EPA's response:

Although sulfoxaflor is classified as 'highly acutely toxic' to saltwater invertebrates based on its 96-h LC_{50} of 0.64 mg ai/L, acute and chronic risk quotients for saltwater invertebrates are well below levels of concern (see Table 32 of the ecological risk assessment). It is noted that the units of the EEC should be expressed as ug ai/L in this table. Therefore, risks to saltwater invertebrates are not anticipated based on this risk assessment. As explained in the response to issue # 3, EPA believes the X-474 degradate should not be part of the residues of concern for ecological risk assessment of sulfoxaflor.

12) Non-*Apis* bees, other beneficial insects, and endangered species

> **Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363)**: The risk assessment's cursory treatment of the risks of sulfoxaflor to the ~4,000 species of native North American bees is unconvincing, a major failure given the severe declines many of these critical species are facing.[59] These bees lack the carefully-bred adaptability and resilient social structures of *Apis mellifera* and many have entirely different life cycles and vulnerabilities. Native species are at a far higher risk from pesticide toxicity than managed colonies of *A. mellifera*. The RA only mentions *Bombus* species in passing, and does not address other native pollinators. Acute oral toxicity to bumblebees is high, although the acute contact toxicity is lower than for honey bees. The oral toxicity of the formulated product is much higher for bumblebees than for honey bees, and toxicity for important native bee species is entirely unknown at this point. These unidentified additional effects on beneficial insect species should further dissuade EPA from registering sulfoxaflor prior to conducting comprehensive pollinator risk assessments.
>
> There are numerous other beneficial insects and other invertebrates that are severely impacted by prophylactic applications of various commercial insecticides. EPA's knowledge of the impacts on these species is far more limited than its knowledge of the impacts on honey bees. Massive data gaps exist for beneficial non-bee insects such as butterflies, ladybugs and lacewings, dragonflies, hoverflies, and others, which are not addressed by the RA.
>
> This section of the sulfoxaflor RA needs dramatic bolstering. If EPA proceeds with the current RA framework it appears likely that beneficial native insects, including rare and endangered species, will face continuing jeopardy. Given that many of these native species have small, localized native ranges, the assessment process should consider the need to restrict or limit the use of sufloxaflor in those locations, a consideration lacking in the document. Otherwise, exposure routes such as foliar spraying could effectively eliminate large portions of remaining populations of native bees and other beneficial insects. Overall, the applicant data submitted to EPA on *Apis* and non-*Apis* bees and other beneficial invertebrates is inadequate and fails to constitute an adequate effects analysis for Federally-listed threatened and endangered species as required by Section 7(a)(2) of the Endangered Species Act. This violates that Act and must be remedied.

EPA's response:

EPA acknowledges that compared to *Apis mellifera*, toxicity data for non-*Apis* bees is in general, much more limited. This is due in large part to the lack of standard toxicity testing protocols and limitations in

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[59] See, for example, Evans E, et al. 2009. Status Review of Three Formerly Common Species of Bumble Bee in the Subgenus *Bombus*, Xerces Society. Available at: www.xerces.org/wp-content/uploads/2009/03/xerces_2008_bombus_status_review.pdf .

availability of *non-Apis* species that are appropriate for regulatory application. However, as described in EPA's recent Proposed for Pollinator Risk Assessment[60], pollen and nectar consumption rates for *A. mellifera* appear protective of those for several non-*Apis* species for which consumption information is known (*e.g.*, European mason bees, alfalfa leaf-cutter bees, bumble bees). Although other exposure routes (*e.g.*, soil) may be more important to certain non-*Apis* bees (*e.g.*, ground nesting bees), the properties of sulfoxaflor and its application method are not expected to result in ecologically significant levels in soil. Specifically, sulfoxaflor is applied as a foliar treatment rather than a soil application. Furthermore, any amount of sulfoxaflor that reaches the soil is expected to rapidly degrade to the X-474 degradate which is practically non-toxic to bees. Regarding pesticide toxicity, EPA is not aware of information that suggests non-*Apis* bees would tend to be more or less sensitive to pesticides compared to *A. mellifera*. Therefore, until toxicity protocols are established and validated for regulatory application with non-*Apis* bees, EPA will continue to rely on risk assessment of *Apis* as a surrogate organism for bees in general. This approach is consistent with the Agency's use of the surrogate species methods for pesticide ecological risk assessment for all other taxa.

EPA appreciates the comment raised regarding endangered species. Based on the risk profile for the proposed uses of sulfoxaflor, the Agency has determined that such registration would result in a "No Effect" determination for listed freshwater and estuarine/marine fish, aquatic invertebrates, and aquatic plants in relation to direct effects on these listed taxa. Similarly, the Agency makes a "No Effect" determination for direct effects on listed terrestrial plants. These 'No Effect' determinations are based on the lack of exceedence of the Agency's acute and chronic risk levels of concern (LOC) for listed species in these taxonomic groups. For listed birds, mammals and terrestrial invertebrates, the acute or chronic listed species LOC values were exceeded for one or more proposed uses. Therefore, the Agency cannot make a determination at this time until the temporal and spatial co-occurrence of listed species with sulfoxaflor use patterns is identified and evaluated.

EPA is currently developing tools that are expected to further refine the assessment and are designed to support effects determinations for individual federally listed species and their designated critical habitats (where applicable). Scientific information obtained from the U.S. Fish & Wildlife Service (USFWS), the National Marine Fisheries Service (NMFS), and other reliable sources is being collated by EPA to address all currently listed species. The information will be stored in an Office of Pesticide Programs Pesticide Registration Information SysteM (PRISM) knowledgebase. The listed species knowledgebase will consist of an information repository that houses biological and behavioral information relevant to individual species (*e.g.*, habitat, diet, and life history, including specific temporal and spatial associations) and a document repository that contains supporting documents (*e.g*., USFWS recovery plans) and electronic information (*e.g*., GIS data files). For terrestrial taxa, the biological information relevant to risk quotient (RQ) calculations (*e.g*., diet and body weight) will be used to parameterize exposure estimates to derive species-specific RQs using a method consistent with currently used methods in the T-REX and T-HERPS models.

Refinements may also include more detailed analyses of the registered uses and their use patterns that result in LOC exceedances for federally listed species in the screening-level assessment. The analyses may include more information on where, when, and how sulfoxaflor is used on selected crops for which LOCs are exceeded. Actual usage data (when available) and national land-cover datasets that indicate potential use sites (*e.g*., national land cover dataset (NLCD), crop data layer (CDL)) may be used to support a more refined analysis of where sulfoxaflor is reasonably expected to be used. Similarly, refinements for the timing of applications and how sulfoxaflor is used may be based on the analysis of additional usage data, beyond what were available at the time of the screening-level assessment, and a more in-depth exploration of agronomic practices.

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[60] available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004

In addition, a committee of the National Research Council (NRC) has been tasked with providing advice on ecological risk assessment tools and scientific approaches under ESA and FIFRA (Project Identification Number DELS-BEST-11-01). The committee has been asked to review the use of "best available data"; methods for evaluating sublethal, indirect, and cumulative effects; the state of the science regarding assessment of mixtures and pesticide inert ingredients; the development, application, and interpretation of results from predictive models; uncertainty factors; and what constitutes authoritative geospatial and temporal information for the assessment of individual species and habitat effects. The Agency recently received the NRC report on April 30, 2013, which is currently being reviewed.

The refinements based on individual species data; additional, detailed usage information, when available; and further recommendations from the NRC report are expected to help to more accurately identify potential areas of effect and to better inform effects and habitat determinations for listed species and any designated critical habitats. For example, if sulfoxaflor is used when a particular species of concern is not present (*e.g.*, it is migratory) or is not co-located in space, then risk of potential direct effects to the species may often be precluded. If LOCs are still exceeded after conducting the refined analyses, further analyses of the potential spatial and temporal co-occurrence of listed species of concern (and any designated critical habitat) may be conducted. The extent of possible refinement in the analyses of spatial/temporal co-occurrence will largely depend on the scale and quality of the available sub-county level use site (*e.g.*, NLCD, CDL) and species location data.

It is further noted that sulfoxaflor is a replacement for a number of insecticide classes (organophosphates, carbamates, pyrethroids and some neonicotinoids) that present greater risks to a wide-range of non-target species than sulfoxaflor; registration of sulfoxaflor should therefore serve to reduce overall risks to such species, including listed species, when users substitute this product for the majority of the available registered alternatives.

13) Mammalian toxicity, the FQPA safety factor, and the interspecies uncertainty factor

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Sulfoxaflor is classified as "suggestive evidence of carcinogenic potential" based on the incidence of tumors and carcinomas in mice and rats. In carcinogenicity studies, increased incidence of interstitial cell tumors was observed but EPA does not consider these to be treatment related due to a lack of dose-response. Tremors, convulsions, hind limb splaying etc were also observed, and EPA also questions the cause of these. Significant hepatocellular adenomas were observed at high doses of sulfoxaflor in rats. Carcinomas and hepatocellular adenomas were seen in mice. Perputial gland tumors, while observed, were difficult to relate to treatment, leading to the agency's classification of "suggestive evidence of carcinogenic potential." Developmental abnormalities (skeletal, neonatal death) were observed in rats, liver weight and enzyme changes, hypertrophy, tumors were also observed in sub-chronic and chronic studies.

Despite this and the need for an outstanding study, EPA believes that data are "sufficient to support reducing the interspecies uncertainty factor to 3X for the developmental effects," even though many of the studies were lacking. One industry study observed that sulfoxaflor affected the fetal, not adult, rat muscle nAChR and that prolonged exposure caused sustained striated muscle contracture resulting in concomitant reduction in muscle responsiveness to physiological nerve stimulation. According to the study, fetal effects were inducible with as little as one day of exposure at the end of gestation, but were rapidly reversible after birth.[61] While sulfoxaflor does have significant measurable neurotoxic

[61] Rasoulpour RJ, Ellis-Hutchings RG, Terry C, et al. 2012. A novel mode-of-action mediated by the fetal muscle nicotinic acetylcholine receptor

activity in mammalian system (mice and rats), it has been concluded that these effects are not relevant to humans. A search of the literature found no other studies evaluating the effect of sulfoxaflor on mammalian systems and so, much is still unknown about this chemical's potency in humans. However, as a chemical whose mode of action involves selective activity at nAChRs like neonicotinoids, sulfoxaflor effects must not be dismissed so easily. For neonicotinoids, excitatory effects on mammalian nAChRs (increasing anxiety behavior) at concentrations greater than 1 μM have been documented, with speculation that this class of chemicals may adversely affect human health, especially the developing brain.[62] [63] One study out of Duke University Medical Center found that gestational exposure to a single, nonlethal dose of imidacloprid produces significant neurobehavioral deficits and an increased expression of pathological alterations in several brain regions of the offspring of Sprague-Dawley rats, at an age that corresponds to early human adolescence. The authors conclude that these changes may have long-term adverse health effects in the offspring.[64]

Even though there are no residential uses at this time, the Food Quality Protection Act (FQPA) safety factor should not be reduced from 10X to 1X, nor should the interspecies uncertainty factor be reduced to 3X since much is still unknown about developmental neurotoxicity. Given the mode of action similarities between sulfoxaflor and neonicotinoids, the higher potency of sulfoxaflor, and its carcinogenic potential, an FQPA safety factor of 10X should be retained.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): Sulfoxaflor's potential mammalian and human toxicity has not been adequately evaluated. In carcinogenicity studies, increased incidence of interstitial cell tumors were observed but EPA does not consider these to be treatment related due to a lack of dose-response. Tremors, convulsions, hind limb splaying, etc. were also observed, and EPA is unsure about the cause of these. Significant hepatocellular adenomas were observed at high doses of sulfoxaflor in rats. Carcinomas and hepatocellular adenomas were seen in mice. Perputial gland tumors, while observed, were difficult to relate to treatment, leading to the agency's classification of sulfoxaflor as having "suggestive evidence of carcinogenic potential." Developmental abnormalities (skeletal, neonatal death) were observed in rats, liver weight and enzyme changes, hypertrophy, tumors were also observed in sub-chronic and chronic studies.

Despite these demonstrated effects, EPA believes that data are sufficient to support reducing the interspecies uncertainty factor to 3X for the developmental effects, even though many of the studies were lacking. One industry study observed that sulfoxaflor affected the fetal, not adult, rat muscle nAChR and that prolonged exposure causes sustained striated muscle contracture resulting in concomitant reduction in muscle responsiveness to physiological nerve stimulation. According to the study, fetal effects were inducible with as little as one day of exposure at the end of gestation, but were rapidly reversible after birth.[65] While sulfoxaflor does have significant measurable neurotoxic activity in mammalian systems (mice and rats), it has been concluded that these effects are not relevant to humans. A search of the literature found no other studies evaluating the effect of sulfoxaflor on mammalian systems and so, much is still unknown about this chemical's potency in humans.

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resulting in developmental toxicity in rats. *Toxicol Sci.* 127(2):522-34.

[62] Kimura-Kuroda J, Komuta Y, Kuroda Y, Hayashi M, Kawano H. 2012. Nicotine-Like Effects of the Neonicotinoid Insecticides Acetamiprid and Imidacloprid on Cerebellar Neurons from Neonatal Rats. *PLoS ONE* 7(2): e32432. doi:10.1371/journal.pone.0032432

[63] Rodrigues KJ, Santana MB, Do Nascimento JL, et al. 2010. Behavioral and biochemical effects of neonicotinoid thiamethoxam on the cholinergic system in rats. *Ecotoxicol Environ Saf.* 73(1):101-7.

[64] Abou-Donia MB, Goldstein LB, et al. 2008. Imidacloprid induces neurobehavioral deficits and increases expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats following in utero exposure. *J Toxicol Environ Health A.* 71(2):119-30.

[65] Rasoulpour RJ, Ellis-Hutchings RG, Terry C, et al. 2012. A novel mode-of-action mediated by the fetal muscle nicotinic acetylcholine receptor resulting in developmental toxicity in rats. *Toxicol Sci.* 127(2):522-34.

However, as a chemical whose mode of action involves selective activity at nAChRs like neonicotinoids, sulfoxaflor effects must not be dismissed so easily. For neonicotinoids, excitatory effects on mammalian nAChRs (increasing anxiety behavior) at concentrations greater than 1 μM have been documented, with speculation that this class of chemicals may adversely affect human health, especially the developing brain.[66] [67] One study conducted at Duke University Medical Center found that gestational exposure to a single, nonlethal dose of imidacloprid produces significant neurobehavioral deficits and an increased expression of pathological alterations in several brain regions of the offspring of Sprague-Dawley rats, at an age that corresponds to early human adolescence. The authors conclude that these changes may have long-term adverse health effects in the offspring.[68] Results such as these should prompt a closer review of sulfoxaflor's potential impacts to mammals.

Even though there are no residential uses at this time, the Food Quality Protection Act (FQPA) safety factor should not be reduced from 10X to 1X, nor should the interspecies uncertainty factor be reduced to 3X since much is still unknown about developmental neurotoxicity susceptibility. Given the mode of action similarities between sulfoxaflor and neonicotinoids, the higher potency of sulfoxaflor, and its carcinogenic potential, an FQPA safety factor of 10X should be retained. Much is still unknown about sulfoxaflor's mammalian toxicity, so EPA should evaluate sulfoxaflor with conservative safety factors.

EPA's response:

The comments express concern about the evaluation that EPA has made regarding the carcinogenicity and developmental effects of sulfoxaflor. The response, below, is aimed at better explaining the Agency's decisions, which were laid out in the human health risk assessment. EPA has evaluated these areas of toxicity separately; therefore, the response is divided into two parts.

Carcinogenicity: The carcinogenic potential of sulfoxaflor was evaluated by the Agency's Cancer Assessment Review Committee (CARC). This group consists of expert toxicologists from across the Agency. In addition to reviewing the work of the lead toxicologist for the risk assessment, the group ensures that determinations of carcinogenic potential adhere to the 2005 Guidelines for Carcinogen Risk Assessment. In the case of sulfoxaflor, the evaluation included guideline studies of carcinogenicity in male and female rats and mice as well as non-guideline studies designed to specifically elucidate the mode of carcinogenic action of the compound. The guideline studies showed increases in liver tumors and preputial gland carcinomas. The data indicated that the liver tumors were treatment related and that the preputial gland carcinomas may have been treatment related. Leydig cell tumors were also observed in these studies; however, their incidence rate was not significantly different from historical control values. Therefore, the Leydig cell tumors were not considered to be treatment related.

EPA has not concluded that there is no cancer risk from exposure to sulfoxaflor. Rather, the Agency determined, in accordance with the guidelines, that (1) there is "Suggestive Evidence of Carcinogenic Potential" for sulfoxaflor, (2) a non-linear assessment of cancer risk from exposure to sulfoxaflor is appropriate and (3) that a chronic assessment will adequately account for cancer as well as non-cancer

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[66] Kimura-Kuroda J, Komuta Y, Kuroda Y, Hayashi M, Kawano H. 2012. Nicotine-Like Effects of the Neonicotinoid Insecticides Acetamiprid and Imidacloprid on Cerebellar Neurons from Neonatal Rats. *PLoS ONE* 7(2): e32432.

[67] Rodrigues KJ, Santana MB, Do Nascimento JL, et al. 2010. Behavioral and biochemical effects of neonicotinoid thiamethoxam on the cholinergic system in rats. *Ecotoxicol Environ Saf*. 73(1):101-7.

[68] Abou-Donia MB, Goldstein LB, et al. 2008. Imidacloprid induces neurobehavioral deficits and increases expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats following in utero exposure. *J Toxicol Environ Health A.* 71(2):119-30.

toxicity. In light of the comments regarding the reduction of the interspecies uncertainty factor to 3X, the Agency notes that the reduction is only for one risk assessment scenario (i.e., acute dietary) and that the interspecies factor is retained at 10X when assessing chronic risk.

Developmental Effects and the FQPA Safety Factor; Reduction of the Interspecies Factor: The Agency is required to apply the additional 10X FQPA Safety Factor to account for potential increased susceptibility of infants and children to the adverse effects of exposure to pesticides. The factor is assumed to be 10X unless, based on reliable data, the Agency can determine that another safety factor is appropriate. When considering reduction of the FQPA Safety Factor, the Agency examines the completeness of the toxicological database, any observed quantitative or qualitative susceptibility observed in that database, the doses and endpoints selected for risk assessment, and the extent to which exposure estimates may underestimate actual exposures. If, after taking those factors into account, there is any residual uncertainty with regard to pre- and/or post-natal susceptibility, then the FQPA Safety Factor is retained at 10X.

In the case of sulfoxaflor, reproduction studies with rats showed developmental abnormalities at low doses. The studies show that the developmental effects could be attributable to a single, *in utero* exposure; therefore, the Agency selected those effects as the endpoint of concern when assessing acute exposure to women of child-bearing age (females 13-49 years of age). The 10X FQPA Safety Factor was reduced to 1X given that:

- The doses and endpoints selected for risk assessment purposes are based on sulfoxaflor's developmental effects observed in the susceptible population group,
- The sulfoxaflor database is complete, including numerous non-guideline mechanistic studies designed to elucidate the mode of action resulting in the observed developmental effects and,
- Exposure estimates are conservative and are not expected to underestimate actual exposure estimates.

When considering these factors in concert, the agency has concluded that there are no residual uncertainties with regard to susceptibility.

As discussed in the human health risk assessment, the mechanistic studies provided evidence that the developmental effects were, in fact, due to a neurological mechanism – specifically, that activation of the nicotinic acetylcholine receptor (nAChR) by sulfoxaflor was causing prolonged muscle contraction in unborn rat pups. The prolonged contractions adversely affected the skeletal system and, in the most severe cases, resulted in death of newborn pups due to asphyxiation. These studies also demonstrated that activation of the nAChR by sulfoxaflor was highly specific to the fetal isoform of the receptor. The specificity of the receptor to activation by sulfoxaflor as well as the differences between rats and humans in the timing of the expression of the fetal and adult isoform types provide strong evidence that the developmental effects being used as the endpoint for risk assessment are not likely to be relevant to humans. Despite the evidence that the mode of action resulting in the developmental effects is not likely to be relevant to humans, out of an abundance of caution, the Agency chose to regulate on the developmental endpoint due to the severity of the effects.

The special mode of action studies provided support for reducing the interspecies factor for risk assessments based on the developmental effects. Specifically, the studies demonstrated significant pharmacodynamic differences (PD) between rats and humans, with respect to binding and activating the nicotinic receptor. The data demonstrate that sulfoxaflor does not elicit a response in the human nAChR at concentrations 500-fold higher than the concentrations eliciting a response in the uniquely susceptible fetal rat receptor. Since humans are clearly not more sensitive pharmacodynamically to sulfoxaflor compared to the rat, reduction of the UF for PD to 1X, which assumes an equal response between humans and rats, is conservative. The agency has, however, retained the 3X pharmacokinetic portion of the interspecies uncertainty to account for potential pharmacokinetic differences between rats and humans.

Thus, HED's retention of a 3X interspecies factor is both protective and conservative.

14) Sulfur allergies

> **J. Roberts' (private citizen) comment (Docket # EPA-HQ-OPP-2010-0889-0032)**: I am allergic to Sulfur and Iodine. I am hoping that this Sulfur based pesticide is not approved, because I'm sure that there are many people like me who would either be made terribly sick by eating these foods treated with Sulfur based pesticide, or would simply have to stop eating them unnecessarily. There is no provision for labeling foods that have been treated with one pesticide or another, so many people would be affected without the ability for them or their physician to understand why.

EPA's response:

Sulfoxaflor does contain a sulfur atom as part of its molecular backbone, and sulfur is also present in a number of metabolites and degradates. Studies available for sulfoxaflor adequately reflect the potential toxicity of the parent and any sulfur-containing metabolites; estimated risk from sulfoxaflor and its metabolites in food and water are well below OPP's level of concern.

15) Impacts on human immune systems and pregnant women

> **J. Watson's (private citizen) comment (Docket # EPA-HQ-OPP-2010-0889-0237)**: The EPA has proposed to register a new insecticide, Sulfoxaflor, which the agency has classified as "very highly toxic" to honey bees. The disappearance and killing of Honeybees has been linked to damaged Honeybee immune systems, which is possibly caused by these toxic insecticides. Not only is there a danger to the honeybees but Sulfoxaflor toxins entering the plant stem, leaves, blossoms, nectar, fruits and vegetables are also sold to consumers and served to families without the ability of the food preparer to wash or remove the pesticides. Therefore, in addition to Bees, Sulfoxaflor may affect the human immune systems, particularly pregnant mothers ingesting the pesticides contained in these plants and passing them on to their unborn children to result in weakened or damaged immune systems which may make them susceptible to diseases from cancer to autism. I propose that the EPA conduct research studies "independent" of those conducted by the pesticide companies to determine if Sulfoxaflor poses a danger to both Bees and humans eating these plants and what effect it has on unborn children whose mothers have eaten these pesticide laden plants. That until a proper and full research studies are performed that the EPA immediately ban the use of Sulfoxaflor.

EPA's response:

As part of its review, the Agency examines studies specifically designed to assess immune function. In addition, the Agency looks for evidence of immunotoxicity, such as effects on the thymus and spleen, in other toxicity studies. There is no indication in any of these studies that sulfoxaflor impacts the immune system of mammals, including humans. Regarding pregnant females, the Agency has reviewed developmental toxicity studies in the rat and rabbit, as well as a reproductive toxicity study and a developmental neurotoxicity study in the rat. These studies assess the impact on both the parental animals and the offspring and therefore endpoints resulting from these studies will be protective of developing offspring and the pregnant females. These studies include gavage and dietary studies, and would reflect dietary exposure to pregnant females. Furthermore, high-end inputs related to dietary exposure, such as use of residue data from field trials, conservatively modeled estimates of residues in drinking water, and an assumption that all of the crops for which registration was sought were, in fact, treated with sulfoxaflor, did not result in risks of concern. The studies submitted by pesticide companies to the Agency for evaluation of sulfoxaflor were conducted in accordance with Good Laboratory Practice (GLP) guidelines and have been accepted by the US, Canada, and Australia. The GLP guidelines are intended to ensure the quality and integrity of data submitted to the Agency and the results of these studies are considered appropriate for use in human health risk assessment. EPA has determined that no additional studies are needed to address the concerns raised in this comment.

16) Impractical and/or unenforceable label statements

Beyond Pesticides' comment (Docket # EPA-HQ-OPP-2010-0889-0384): Sulfoxaflor's proposed label statements attempt to warn the user of the risks to bees. However, these labels seem to be unrealistic in the real world and unenforceable. Statements advising users to make applications before 7.00am or after 7.00pm ignore EPA's own data that the product is still highly toxic up to three days after application. While spraying before and after bees are active in fields may minimize direct contact exposures, residual exposures, at least up to three days, are still highly toxic and do not solve the problem of minimizing risks.

Other label statements that are currently in use include: "Do not apply during bloom"; "Do not apply three days prior to bloom…"; "Do not make more than one application...three days prior to bloom" etc. These have not been practical or enforceable. The agency is aware that label directions such as these are not adhered to in the real-world. Many beekeepers can attest to this. Addressing lack of compliance has been an area the agency has not sufficiently addressed throughout the years. These labels are also unenforceable. Moreover, instructions to minimize pesticide drift continue to be a challenge especially for aerial applications.

Meanwhile, EPA and state enforcement capabilities seem to be almost non-existent. Many states do not have the resources or manpower to enforce product labels, collect incident data, or conduct necessary inspections. Given the challenges that exist with product label compliance, and the declines in bee populations in the U.S., the agency must reconsider granting registration to a product with such high risks to bees without the proper safeguards in place.

National Pollinator Defense Fund's comment (Docket # EPA-HQ-OPP-2010-0889-0369): Protection of pollinators from sulfoxaflor poisonings requires that label restrictions be enforced, yet the discussions within the PPDC Pollinator Workgroup have made it clear that enforcement at the state level is dysfunctional in many states. Label statements are confusing and undefined, and the State Lead Agencies in charge of enforcement believe them to be unenforceable. The result is that readily preventable acute bee kills still happen with regularity and with impunity for those causing the kills. EPA can solve this problem by clarifying label language and ensuring that states require mandatory training in pollinator protection for applicators and require state regulators to take their enforcement mandate seriously by acting expeditiously to fully investigate each incident, document the incident in a traceable manner, file a comprehensive report of the incident with US EPA, and take corrective action to avert future poisoning incidents.

Thomas R. Smith's comment (Docket # EPA-HQ-OPP-2010-0889-0342): 5. The Environmental Section mandatory language as it pertains to pollinators for the Sulfoxaflor label will not be followed by applicators nor enforced by State Lead Enforcement Agencies. This is the current situation for existing pesticide labels. This fact has been reported by the beekeeping industry to EPA during the PPDC discussions and by past industry leaders for decades. This fact is also substantiated by State Lead Agencies stating in the PPDC work group session, on more than one occasion, that the current mandatory label language does not consist of "legal" terms. It is common knowledge that EPA has not defined the mandatory terms. It is also documented that the request for definitions has gone unanswered for decades. State Lead Agencies have stated that the mandatory terms cannot be determined in the field therefore they not enforceable. In practice the Environmental Section is deemed as Advisory language in the eyes of applicators and State Lead Enforcement Agencies. There is no evidence that the Mandatory language for Sulfoxaflor would be followed based upon this evidence.

6. The vast majority of Sulfoxaflor applications will occur as other pesticide applications are presently occurring. In crops which are not dependent upon pollinators, the applications will begin at sunrise and end at sunset resulting in unacceptable damage to pollinators exposed to direct contact and highly contaminated pollen. Applications will occur in similar fashion for crops which require pollination when managed pollinators colonies are not present in the field under contract. Applicators will follow the Mandatory language when managed pollinator colonies are present in the field under contract. Sadly native pollinators will suffer when managed colonies are not present and under contract.

The Section 18 Permit utilized a beekeeper written notification as the risk mitigation measure to protect managed honey bee colonies. In reality this was a notice for beekeepers to move their colonies and place them where another farmer will have to protect them. Notification is not a mitigation measure. Notification programs are not acceptable to the commercial honey bee industry, as has been stated in the PPDC work group's records and the PPDC meetings. Moving colonies to facilitate pesticide applications is not a sustainable business or colony management model. Managed pollinators and the majority of native pollinators must reside near good soils with adequate rainfall or irrigation. The poor soils lacking adequate water will not sustain the pollinators or production agriculture. The two are forced to coexist. It will be of no value for EPA to include a notification requirement on the Sulfoxaflor label. The bees will not be moved. They will just be damaged.

The only possible recommendation I can provide is for EPA to include clear Advisory language which will define the Mandatory language intent. Including how long Sulfoxaflor will kill bees in the different crops in bloom if the Mandatory language is followed. Also provide the expected damage to pollinators if the Mandatory language is not followed and applications are made as I expect, from sunrise to sunset to blooming crops.

The proposed label language states application be completed before 7:00 hours AM and after 7:00 PM. My first question would be: Is these times Mandatory? Second question: Is the language adequate to dispel confusion concerning Daylight Savings Time? For the sake of example, I will assume the language is adequate to describe the sunrise/sunset tables published in the newspaper. Let's assume the median cotton belt latitude is Dallas, Texas. Also for this example, let's assume adequate natural light exists to safely operate all application equipment for 30 minutes before sunrise and 30 minutes after sunset. On July 1, 2013 in Dallas, Texas the sunrise occurs at 6:23 AM and sets at 8:39 PM. Providing for 30 minutes before and after sunrise and sunset the time for which adequate light will exist the label language would define applications times as:

5:23 to 7:00 AM = 1 hour 7 minutes
7:00 to 9:09 PM = 2 hours 9 minutes
Totaling 3 hours 16 minutes daily

My points of this example are:
1. Honey bees will absolutely be exposed to direct contact based their habits and the defined language application times.

2. It has been reported and documented in the PPDC workgroup session that the official position of the Aerial Applicators is that night applications are not safe. (This position does not reflect that aerial night applications have been practiced in many areas since the 1970's and are standard practice when bees are located in pollination fields .)
3. It has been voiced by the Cotton Council that ground application equipment also cannot safely be operated at night in the PPDC work group meetings.
4. The total daily defined application period of 3 hours 19 minutes will not be observed by applicators. The expectation of applicators to prepare for only 1 hour and 7 minutes in the morning and return for 2 hours 19 minutes in the late afternoon will be considered absurd!
5. EPA must be assume, based on this information, that applicators will apply Sulfoxaflor from first light to sunset. State Enforcement Agencies will be influenced by political pressure and allow applications to occur by deeming the label language "Advisory".
6. EPA can only conclude the pollinators will be directly exposed to and, severely damaged by, Sulfoxaflor applications.

Center for Food Safety's comment (Docket # EPA-HQ-OPP-2010-0889-0363): There are several areas where EPA suggests potential mitigation efforts for certain crops to reduce pollinator exposure (e.g., timing applications for late in the day for cucurbits), but these are only offered as voluntary applicator practices, not requirements. On the proposed label, application is required to avoid bloom periods for certain crops, but this is not adequate to protect pollinators from pre-bloom applications because of the systemic nature of sulfoxaflor. These mitigation efforts also do not reduce the likelihood of bees contacting sulfoxaflor via drift on to neighboring lands, and essentially ignore the higher exposure likelihood on the day of application. The systemic nature of sulfoxaflor and its major degradates means that these suggested mitigation measures will not be adequate to protect honey bees and other pollinators from exposures.

EPA's response:

EPA has proposed mitigation measures for sulfoxaflor which include lowering application rates and lengthening the interval between applications. These mitigation measures are mandatory and therefore enforceable. The label also includes the mandatory prohibition against application prior to bloom, during bloom and until after petal fall for a number of crops. These statements are mandatory and enforceable. Advisory statements regarding making applications in the early morning and late evening, and when the temperature is <55˚F, will inform growers of additional steps they can take to minimize exposure to foraging bees. Additionally, EPA agrees with commenter #0342 that notification is not a mitigation measure, however, the sulfoxaflor label will include a recommendation that beekeepers in the area be notified of planned applications so that beekeepers may be informed and communication and coordination between growers and beekeepers may be enhanced.

Commenters state that enforcement capabilities at the state and Federal level are nonexistent due to reduced resources and poor labeling. They also state that the Agency is aware that label directions are not adhered to. There is some degree of misuse in all commodities and instances where applicators have willfully ignored label restrictions or used unauthorized pesticides. In fact, EPA has taken enforcement action for misuse in numerous situations such as adulteration of crops (ex. misuse of zeta-cypermethrin on wheat in multiple states in 2001) and when spray drift has caused adverse effects (ex. clomazone damage to residential properties). EPA is aware that beekeepers themselves have resorted to the use of unregistered miticides and other compounds to combat Varroa mites and other hive pests. However, EPA believes that most growers and beekeepers apply pesticides according to the approved labeling. Furthermore, because bee kill incidents are unique, EPA is collaborating with states, with input from pollinator experts, in order to develop guidance to assist inspectors to better investigate alleged bee kill incidents.

Registration of sulfoxaflor is expected to replace multiple applications of older chemistries (ex. organophosphates, pyrethroids) and will displace applications of compounds in other neonicotinoid subgroups. Therefore, sulfoxaflor is not expected to present an additive risk scenario for pollinators. Additionally, as noted by the National Pollinator Defense Fund, the PPDC Pollinator Workgroup is working on improving pollinator protective label language. Many older pesticide products have less restrictive and informative language than sulfoxaflor.