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Proposed Registration of Isocycloseram (Plinazolin®)

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Docket ID No. EPA-HQ-OPP-2021-0641
U.S. Environmental Protection Agency
Office of Pesticide Programs
1200 Pennsylvania Avenue, NW
Washington, DC 20460
RE: Comments on Proposed Registration of Isocycloseram (Plinazolin®)

Introduction and Purpose

The Arizona Pest Management Center is host to the University of Arizona's expert IPM scientists, including Ph.D. pest management specialists with expertise in the strategic tactical use of pesticides within Integrated Pest Management (IPM) programs that protect economic, environmental and human health interests of stakeholders and society at large. As part of a larger regional collaboration with the Western IPM Center at UC Davis, we monitor the Federal Register and frequently submit comments on EPA pesticide registration reviews or other topics impacting agricultural and nonagricultural stakeholders, including pesticide use, IPM, and related issues in the Desert Southwest.

On behalf of the Arizona Pest Management Center (APMC), we submit these comments regarding the proposed registration of the new active ingredient isocycloseram (Plinazolin®) as published in the Federal Register under Docket ID EPA-HQ-OPP-2021-0641. Our Center represents the University of Arizona's statewide Integrated Pest Management (IPM) programs and stakeholders across the desert Southwest, including growers, pest control advisors, and research and Extension professionals. While our comments represent a primary interest in isocycloseram as an important new pest management option in Arizona cotton, we wish also to call EPA's attention to comments submitted earlier in the comment period on behalf of Dr. John Palumbo, which address uses in vegetable crops of the desert Southwest.

We appreciate EPA's rigorous assessment of this new chemistry, and we commend the Agency's efforts to balance ecological protection with grower needs. We offer these comments to support Plinazolin's registration and to recommend adjustments to proposed bloom-time and buffer restrictions that could otherwise limit its usefulness in our systems.

1. Plinazolin's Unique Role in Arizona Cotton IPM

We conducted extensive field research on isocycloseram (Plinazolin) in the Arizona cotton system in 2020, 2021 and 2023 to evaluate efficacy of isocycloseram and non-target impacts[1]. Our approach to these evaluations included field tests for efficacy, measuring non-target effects of applications on more than 27 arthropod taxa, including twelve natural enemies, six of which are key whitefly predators in our system that contribute to biological control[2,3]. We identified abundance of species, calculated predator : prey ratios, conducted *in situ* sentinel prey removal, and examined food web dynamics using principal response curves (PRCs) to show mean effects of insecticides on the arthropod community[1] (Figure 1). Predator abundance is shown in Figure 2.

Plinazolin is the first new insecticide mode of action targeting Lygus for Arizona cotton in over a decade. We have included Plinazolin in our 2025 Cotton Insecticide Use Guide[4] (not yet registered) based on rigorous field evaluations that demonstrate:

- High efficacy against *Lygus hesperus*, the number one yield-limiting pest of cotton in Arizona and California.
- Collateral control of mites, reducing secondary pest outbreaks; and putative control of stink bugs, especially *Eushistus servus* for which we have no effective and selective chemistries.
- Partial selectivity to key natural enemies, particularly four of the six most critical generalist predator groups in Arizona cotton agroecosystems[1].
- A favorable environmental and ecotoxicological profile compared to older chemistries.

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[1] Bordini, I., S. Naranjo, A. Fournier, P. Ellsworth. 2024. Determining Selectivity of isocycloseram and afidopyropen and their Compatibility with Conservation Biological Control in Arizona Cotton. Pest Management Science. Article ID: PS8460. October 2024. https://doi.org/10.1002/ps.8460

[2] Bordini I, Ellsworth PC, Naranjo SE and Fournier A, Novel insecticides and generalist predators support conservation biological control in cotton. Biol Control 154:104502 (2021).

[3] Vandervoet TF, Ellsworth PC, Carrière Y and Naranjo SE, Quantifying conservation biological control for management of *Bemisia tabaci* (Hemiptera: Aleyrodidae) in cotton. J Econ Entomol 111:1056–1068 (2018). https://doi.org/10.1093/jee/toy049.

[4] Bordini, I.C., A.J. Fournier, S.E. Naranjo, N.M. Pier, P.C. Ellsworth. 2025. Cotton Insecticide Use Guide: Knowing and Balancing Risks. IPM Short. University of Arizona Cooperative Extension, Arizona Pest Management Center. http://hdl.handle.net/10150/676898

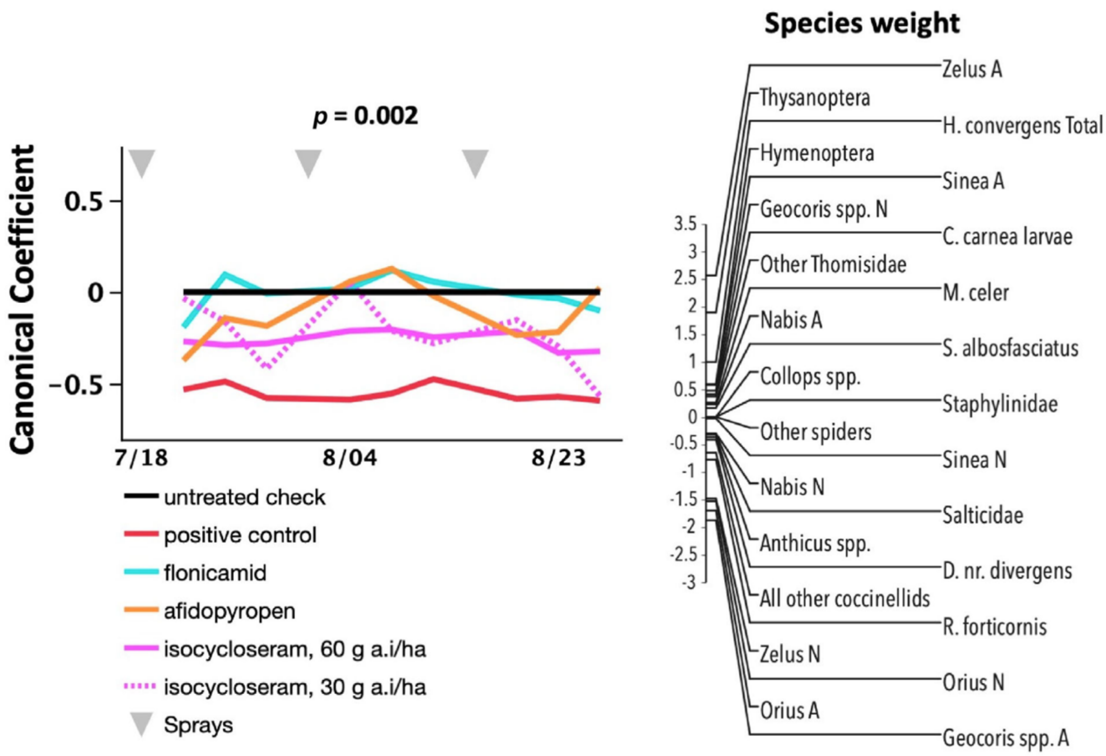

Figure 1. Principal response curves (PRCs) showing the main effects of insecticides on the arthropod community relative to the untreated check (y = 0 line) in 2023 in Maricopa, AZ (P = 0.002); Species Weights on right. A, adults; N, nymphs.

Plinazolin for Lygus Management

In Arizona, there are currently three options that provide excellent control of Lygus bugs, two that are fully selective and safe for natural enemies, and therefore preferred by producers, and oxamyl, which is broad spectrum and non-selective. Another option with good efficacy is acephate, but it, too, is broad spectrum and discouraged because of the potential for secondary outbreaks of mites and whiteflies. As a result, acephate is used <5% of the time when targeting Lygus. The balance of sprays against Lygus bugs are split between flonicamid and sulfoxaflor. Indoxacarb is available for suppression of Lygus when otherwise targeting lepidopteran pests, especially in non-Bt cottons like Pima cotton. In California, the list of alternatives for Lygus control are similar to Arizona. However, sulfoxaflor is unavailable there, and both novaluron and pyrethroid mixtures and neonicotinoids are often also used.

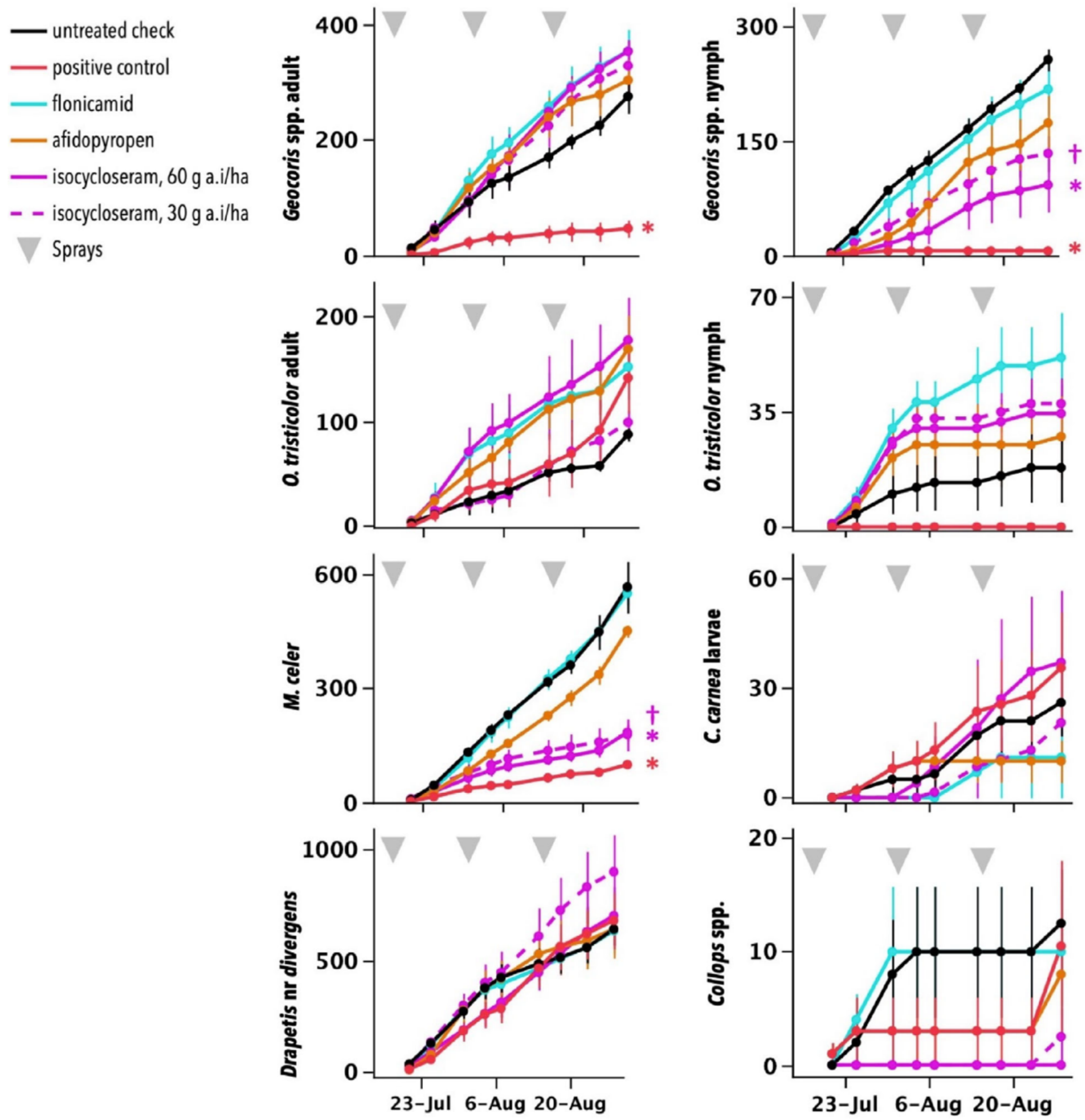

Figure 2. Post-treatment, cumulative mean insect-days (error bars = SE) for arthropod predators per 100 sweeps in 2023. Statistical analyses were conducted on abundance for a given date. Asterisk and cross colors correspond to treatment seasonal means for insecticides that were significantly different from the untreated check by Dunnett's, $P < 0.05$. Note that for *D.* nr *divergens* only, the interaction Insecticide × Date was significant ($P < 0.05$). The abundance of *D.* nr *divergens* was significantly higher in acephate compared to the untreated check in the sixth sampling date by Dunnett's, $P < 0.05$ (not shown on chart).

In years when lygus populations are high in cotton, more than two applications may be needed to adequately maintain yields. This can lead to the use of broadly toxic insecticides such as oxamyl, which negatively impacts populations of beneficial predatory arthropods in cotton, often leading to the need for additional sprays to control lygus or whiteflies. Acephate is also used at times to similar effect. Isocycloseram, given its generally favorable profile for preserving four out of six key predator specie groups in cotton[3], will be a welcome and valuable tool for lygus management in our cotton IPM program.

Plinazolin for Stink Bug control

For the most part, stink bugs have not been a major pest in the Arizona cotton system. However, starting in 2012, the brown stink bug, *Euschistus servus* Knight, broke out in Arizona cotton for the first time since 1961. Although native and occasionally present at very low levels, it was an unfamiliar pest and the industry was uncertain how much damage was occurring or how to control the brown stink bug. Research and Extension guidelines from the southeastern US suggested that the pyrethroids bifenthrin and zeta-cypermethrin and the organophosphate dicrotophos were particularly effective, the latter lacking a state registration in Arizona. By 2013 that state label was installed and growers began using dicrotophos, although some continued usage of pyrethroids because of the highly hazardous nature of the organophosphate. After two years of significant use, new research demonstrated the futility of these chemical controls for brown stink bug in Arizona[5]. What little efficacy there was against brown stink bug failed to produce increases in yield or quality and exposed the grower to predictable losses from secondary outbreaks of mites and resurgent whiteflies, driven by a reduced presence of natural enemies. By 2015, almost no one was using dicrotophos and pyrethroid use had again declined. However, over the course of this period the average number of sprays made to cotton doubled.[6]

Isocycloseram has not been specifically tested in Arizona for efficacy against stinkbugs—there is, however, data supporting this use from elsewhere in the southeastern cottonbelt. It could prove valuable as a tool for occasional outbreaks of the brown stink bug or other stink bugs in cotton and other crops in Arizona and the West.

Plinazolin for Mite Control

Although we do not spray often for mites in Arizona cotton, abamectin is a primary chemistry of choice here, due to efficacy and price. It is also important for mite control in California and across the cotton belt[7]. Abamectin has been identified as a Highly Hazardous Pesticide (HHP) by international agreements and is very damaging to natural enemy populations. Etoxazole (Zeal) is an available selective option for mites, though there is little use of this in Arizona. It has been noted in Arizona (and perhaps elsewhere) that ThryvOn cotton, genetically modified to provide control of Lygus and thrips may be more prone to significant damage from mites. This is likely due to ThryvOn efficacy against Western flower thrips, which is also a predator and can help

[5] Brown LM, Biology, Ecology, and Economics of Brown Stink Bug, Euschistus Servus (Heteroptera: Pentatomidae), in Desert Cotton Agroecosystems (Masters thesis. The University of Arizona), Tucson, AZ (2017) Available at: http://hdl.handle.net/10150/625340 (accessed 10 May 2025).

[6] Ellsworth, P.C., A.J. Fournier. 2025. Insecticide Mixtures for Pest Management or Resistance Management in Arizona Cotton. Pest Management Science. Vol. 81, no. 3, March 2025. https://doi.org/10.1002/ps.8241

suppress mite populations. Isocycloseram may have a significant role to play in mite management in Arizona and other states, across a variety of cropping systems.

<u>All these factors</u> place Plinazolin in a utility class above potentially widely used but disruptive organophosphates (OPs) like acephate and dicrotophos pyrethroids, abamectin, novaluron, or oxamyl, which historically have triggered pest resurgence and secondary outbreaks due to their broad toxicity[7],[8].

2. Resistance Management Imperatives

Isocycloseram is classified by the Insecticide Resistance Action Committee (IRAC) as a Group 30 insecticide (IRAC, 2025) and will represent the first foliar Group 30 option providing a new mode of action for resistance management. This combined with its wide spectrum of target pest control makes it a very welcome tool for integrated resistance management programs across diverse crops nationwide. Also, there is no known resistance or cross-resistance to isocycloseram and so it will help break resistance for certain pests that have or can become resistant to currently available registered insecticides. In Arizona cole crops including broccoli, cabbage and others this will be extremely important for diamondback moth. In recent years, growers have seen troubling levels of resistant diamondback moth on transplanted brassica crops in Southwestern Arizona.

Since 2006, Arizona cotton growers have relied heavily on Carbine® (flonicamid) and, more recently, Transform® (sulfoxaflor) for selective Lygus control[9]. With over 15 years of near-exclusive dependence on these two chemistries, the risk of resistance is elevated. Plinazolin offers a much-needed rotational partner for lygus control, especially important in Arizona's long cotton growing season, which can exceed 180 days with an extended bloom period. Transform is not registered in California, making Plinazolin even more critical as a non-organophosphate and non-neonicotinoid alternative in Western production systems.

3. Bloom Restriction Concerns

EPA has proposed a prohibition on Plinazolin applications for indeterminant-blooming crops during bloom unless conducted before 10 a.m., after 3 p.m., or when ambient temperatures are

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[7] Brown, L.M. 2017. *Biology, Ecology, and Economics of Brown Stink Bug,* Euschistus servus *(Heteroptera: Pentatomidae), in Desert Cotton Agroecosystems.* M.S. Thesis, Department of Entomology, University of Arizona. https://repository.arizona.edu/handle/10150/625340

[8] Fournier, A., Ellsworth, P.C., Palumbo, J.C., Peña, M., & Dixon, W. 2022. *Response to EPA Notice: Petition to Revoke Tolerances and Cancel Registrations for Certain Organophosphate Uses.* Arizona Pest Management Center, University of Arizona. https://acis.cals.arizona.edu/docs/default-source/ipm-assessment-documents/arid-swpmc-info-requests/comment-reponses/op-tolerance-revocations_apmc_09-25-22_vf.pdf

[9] Ellsworth, P.C., A.J. Fournier. 2025. Insecticide Mixtures for Pest Management or Resistance Management in Arizona Cotton. Pest Management Science. Vol. 81, no. 3, March 2025. https://doi.org/10.1002/ps.8241

below 50°F. We strongly urge EPA to reconsider this restriction for cotton, for the following reasons:

- Cotton is not a pollinator-attractive crop per EPA's 2017 pollinator protection policy[10],[11]. Further, we concur with comments submitted to this docket by USDA Office of Pest Management Policy that state this restriction in indeterminant-bloom crops is likely unprecedented and contradicts EPA's previous determinations for the likelihood of bees foraging in these crops.
- Because EPA's 2017 policy is scientifically defensible and provides a well-established framework for on-field mitigations, USDA-OPMP expressed concerns about this decision falling outside of the previous precedent, especially given the low risk of isocycloseram relative to most of the alternative chemistries that do not have such restrictions in place. No such restrictions apply to many organophosphates, pyrethroids, or other older broad-spectrum chemistries which disrupt biological control. Inclusion of this label language will create a perverse incentive for growers to use more disruptive products.
- Arizona's extended bloom and high Lygus pressure often require action during peak bloom periods.
- Based on our extensive field evaluations, beneficial arthropods that consume pollen and nectar from cotton flowers tolerate Plinazolin well[1,2] ensuring continuity of biological control services even during bloom.

4. Buffer Zone Restrictions and Practicality

EPA's proposed wind-directional spray drift buffers are generally consistent with the Insecticide Strategy, accounting for the presence of managed areas downwind from a spray and the flexibility to reduce buffer distances based on options from EPA's Mitigation Menu website. We think this consistency is important for growers. We have been actively training growers and pest control advisors on the ESA Strategy mitigations, and consistency is important for compliance and to avoid confusion. We are concerned with EPA's proposed mandatory non-wind-directional spray drift buffers for aquatic areas. These lack mitigation flexibility and offer no means for reduction (e.g., through drift-reduction technologies). This diverges from the EPA's Insecticide Strategy framework, which encourages flexible, context-driven mitigation. We encourage alignment with the Insecticide Strategy to ensure feasible, IPM-compatible implementation. Furthermore, as USDA Office of Pest Management Policy has stated in their comments to this docket, it is unclear why the aquatic buffers are different, that is, why the wind-

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[10] EPA. 2017. U.S. Environmental Protection Agency's Policy to Mitigate the Acute Risk to Bees from Pesticide Products. U.S. Environmental Protection Agency. EPA-HQ-OPP-2014-0818-0477. https://www.regulations.gov/document/EPA-HQ-OPP-2014-0818-0477

[11] USDA. 2018. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen. U.S. Department of Agriculture. https://www.usda.gov/sites/default/files/documents/Attractiveness-of-Agriculture-Crops-to-Pollinating-Bees-Report-FINAL-Web-Version-Jan-3-2018.pdf

directional buffers alone are deemed insufficient to address ecological concerns. The existence of two types of buffers with different guidelines for implementation on a single label is likely to be confusing for growers. Unless strong justification for a second set of buffer requirements can be made, we urge EPA to eliminate the non-wind-directional spray drift buffer requirement.

The proposed minimum buffer distance of 300 feet for the wind-directional aerial spray drift buffer seems extreme, given isocycloseram's low-risk profile. While EPA's benefit analysis supports the retention of aerial applications on cotton and a few other crops, we are concerned that this large buffer distance will make Plinazolin unworkable for many growers.

5. Summary and Recommendation

Plinazolin represents a critically needed tool for Arizona cotton production. Its partial selectivity, new mode of action, and eco-friendly profile position it as an ideal candidate to displace older, high-risk chemistries. While well-intentioned, the proposed bloom and buffer restrictions could undercut this value and lead to worse outcomes for pollinators and non-target organisms by driving growers to older, more harmful products especially should resistances develop in Lygus.

We respectfully request that EPA:

- Remove or revise bloom restrictions for cotton based on existing policy and exposure data.
- Permit drift mitigation flexibility consistent with the EPA Insecticide Strategy.
- Finalize registration to allow Arizona and other cotton-producing states to benefit from this important IPM-compatible technology.

Who We Are

Dr. Al Fournier is Associate Director of the APMC / Associate Specialist in Entomology, holds a Ph.D. in Entomology, and has expertise in evaluating adoption and impact of integrated pest management and associated technologies. He works with the Western IPM Center, representing stakeholders in the desert Southwest states in EPA registration reviews. Dr. Peter Ellsworth is Director of the APMC, State IPM Coordinator for Arizona and Professor of Entomology / Extension IPM Specialist with expertise in developing IPM systems in cotton and other crops and measuring implementation and impact of IPM and pest management practices.

These comments are the independent assessment of the authors and the Arizona Pest Management Center as part of our role to contribute federal comments on issues of pest management importance and do not imply endorsement by the University of Arizona or USDA of any products, services, or organizations mentioned, shown, or indirectly implied in this document.

Thank you for considering these comments. Please feel free to contact us if you have further questions.

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