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PAN
PESTICIDE ACTION & AGROECOLOGY NETWORK

June 10, 2025

Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460-0001

Re: Public Participation for Isocycloseram [EPA-HQ-OPP-2021-0641]

Dear Madam/Sir,

These comments are submitted on behalf of Beyond Pesticides, Pesticide Action & Agroecology Network (PAN), and the 19 undersigned organizations. Founded in 1981 as a national, grassroots membership organization that represents community-based organizations and a range of people seeking to bridge the interests of consumers, farmers, and farmworkers, Beyond Pesticides advances improved protections from pesticides and alternative pest management strategies that eliminate a reliance on pesticides. Beyond Pesticides' membership and network span the 50 states and the world. PAN North America works to create a just, healthy, and equitable food system and is one of five regional centers cooperating to transform food systems across the globe. We are writing regarding the U.S. Environmental Protection Agency's (EPA) proposed registration decision for ten products containing the new active ingredient isocycloseram.

EPA should not register any products with this active ingredient, as it is a PFAS and presents risks of adverse health and environmental effects. Based on isocycloseram's structure, with one of the carbons fully fluorinated as a trifluoromethyl group, the compound falls under the widely accepted definition of the class of chemicals known as per- and polyfluoroalkyl substances (PFAS).[1,2] This definition is utilized by EPA and other associations as a basis for risk assessments for compounds that all fall into this class of 'forever chemicals.' Isocycloseram also contains a dichloro-fluorophenyl group that is of concern.

Toxicity and endocrine disruption concerns of isocycloseram and its degradates

In EPA's "Drinking Water Exposure Assessment for the New Active Ingredient Isocycloseram," it is noted that isocycloseram has 24 major and four minor degradates that could move into adjacent water and cause contamination. The assessment states: "Residues of concern include parent, SYN549431, SYN549107, SYN549546, SYN549433, SYN551190, SYN550737, SYN550602, SYN550603, SYN550455, SYN549110, and SYN551057. Degradates vary in their mobility and persistence."[3]

The toxicity of these residues, and additional metabolites/degradates of isocycloseram, were also analyzed, showing that: "Isocycloseram produced plausible alerts for carcinogenicity and skin sensitization, and an equivocal alert for nephrotoxicity. Thirteen of the metabolites (SYN549107, SYN549431, SYN549433, SYN549546, SYN550455, SYN550602, SYN550737, SYN550738, SYN551030, SYN551113, SYN551190, SYN551324, SYN551485) shared the same carcinogenicity/skin sensitization/nephrotoxicity profile as the parent compound, while five of the remaining metabolites (SYN548569, SYN549543, SYN549554, SYN551203, SYN551478) had two of the three. Six metabolites (SYN549433, SYN549554, SYN550455, SYN550602, SYN551113, SYN551190) produced plausible alerts for glucocorticoid receptor agonism, along with equivocal alerts for teratogenicity (based on the glucocorticoid receptor activity). The epoxide (SYN551324), an environmental degradate, resulted in the three common alerts to the parent compound, along with three additional plausible alerts not shared by any other metabolite for developmental toxicity, eye irritation, and skin irritation."[4]

Numerous studies document exposure to endocrine-disrupting pesticides (EDPs), including PFAS, leading to interference with the endocrine system as well as additional health effects such as cancer, brain and nervous system disorders, immune system disorders, diabetes, learning/developmental impacts, and sexual and reproductive dysfunction.[5] In a literature review published in *Ecotoxicology and Environmental Safety* earlier this year, the authors highlight a multitude of studies on endocrine disrupting chemicals (EDCs) and EDPs showing epigenetic effects from exposure, as the chemicals imitate the action of endocrine hormones and lead to gene damage and multigenerational adverse effects to health.[6]

In summarizing these results, the researchers state, "As a class of particularly representative endocrine-disrupting chemicals, the accumulation of per- and polyfluoroalkyl substances potentially leads to adverse health effects, including hormonal disruptions, developmental issues, and cancer."[6] EPA should not register isocycloseram because it has not addressed the many complex mechanisms that are not yet fully evaluated by the agency.

Concerns over high toxicity to aquatic organisms

Based on the data indicating isocycloseram's high toxicity to aquatic organisms, EPA should not register this pesticide. A label for Isocycloseram Technical, states: "This pesticide is toxic to fish and highly toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority."[7]

This warning highlights the threats to aquatic organisms and echoes the risks to wildlife included in EPA's "Memorandum Supporting Proposed Decision to Approve Registration for the New Active Ingredient of Isocycloseram."[8] The document says the following:

- Isocycloseram is categorized as highly toxic to fish (and aquatic-phase amphibians for which freshwater fish serve as surrogates) on an acute exposure basis.
- Isocycloseram is categorized as very highly toxic to aquatic invertebrates on an acute exposure basis.
- For terrestrial invertebrates, the available data indicate that technical grade isocycloseram is highly toxic both on an acute (single dose) oral and contact exposure basis to honey bee (*Apis mellifera*) adults and larvae, which serve as surrogates for both *Apis* and non-*Apis* bees.
- Isocycloseram is categorized as slightly toxic to birds (and reptiles and terrestrial-phase amphibians for which birds serve as surrogates) on both an acute oral and sub-acute dietary exposure basis.

Another unacceptable risk to wildlife, especially pollinators, is in the proposed registered use of isocycloseram in seed coatings. EPA should not register any isocycloseram seed coating uses because 1) pesticide seed coatings are prophylactic and their use as pesticides is not in response to an existing pest pressure, which can lead to pesticide resistance and escalating use, and 2) use of isocycloseram seed coatings will result in surface water contamination with a pesticide that is highly toxic to aquatic organisms. Finally, seeds coated in pesticides are a hazardous waste disposal problem if they are not planted—yet, when they are planted, the problem is assumed by EPA to be solved, even though the pesticides in seed coatings will contaminate surface water runoff and soil.[9] Because of this, EPA should not register any pesticide seed coatings.

Unacceptable risks to human health: Data gaps on worker exposures from seed treatments and drinking water contamination

The proposed products containing isocycloseram are being registered for use in agriculture, as well as on commercial and residential turf, ornamental plants, vegetable plants, fruit and nut trees, vines, and even as a gel bait for cockroaches. On the label for one product, Equento™ 400FS, there are additional PPE requirements that are not usually included. The label states that for canola seed treatment, workers must wear a minimum of a NIOSH-approved particulate-filtering facepiece respirator, which raises health and safety concerns for seed treatment workers.[10]

Seed treatment worker risks were discussed in the Human Health Risk Assessment, which indicates that EPA does not have data on exposure from use of “open loading systems,” nor does EPA know whether these systems are used for commercial seed treatment.[11] EPA states that “HED [Health Effects Division] anticipates that the risk estimates may be higher…” Based on this statement, the risk to workers has not been appropriately assessed by EPA for a new pesticide registration. EPA should determine whether open loading systems are used in commercial seed treatment, and if these systems are used, HED should collect data to quantify exposure to workers from using open loading systems for seed treatments.

Seed treatment usage of isocycloseram will result in contamination of surface water, as its use on seeds will result in runoff contamination, and other uses are also likely to allow for further movement into water, e.g., via spray drift. EPA stated that it does not know what the effects of water treatment would be on drinking water concentrations of isocycloseram, which means that registration of the pesticide could result in contamination that water utilities will then have to address, potentially at great cost to already-underresourced communities.[3] EPA should not register any seed treatment uses of isocycloseram, given the unknowns with drinking water contamination, risks to workers, and risks to aquatic organisms as noted above.

Chemical residues are persistent in food and drinking water, with over 6 million U.S. residents regularly encountering drinking water with PFAS levels above the EPA health advisory of 70 ng/L.[12] PFAS are detectable in almost all of the U.S. population—disproportionately afflicting people of color communities, which has been documented in California—and have implications for human health.[13]

EPA found that the highest chronic dietary risks are for children 1-2 years of age, whose exposure is estimated at 67% of the Chronic Population Adjusted Dose (cPAD). This very high cPAD, in addition to the cumulative exposures to other pesticides in food, poses an unacceptably high level of risk for children. Given the proposed uses on foods of which children consume relatively copious amounts (vegetables, pome fruits, stone fruits and citrus), EPA should protect children's health by not registering isocycloseram.[14]

In the Human Health Risk Assessment, toxicology studies in mammals reveal threats to reproduction and organs such as the liver, with the most sensitive effect on male reproduction—namely reduced sperm count and testicular degeneration. The assessment states: "Tubular degeneration of testes, and cellular debris and reduced sperm in the epididymides were observed in subchronic, chronic/carcinogenicity, and one-generation reproduction studies in rats. Additionally, hepatocyte vacuolation and/or inflammatory cell infiltrate were noted in the chronic/carcinogenicity and one-generation reproduction studies in rats. Decreased body weight and poor clinical conditions (vomiting and slight body tremors) were observed in dogs after subchronic exposure."[11] These risks to human health, especially to children, are unreasonable and require that EPA not register isocycloseram.

EPA is behind the curve on PFAS and widespread PFAS contamination

Given what is known to EPA and findings in the independent peer reviewed, scientific literature, all PFAS should be banned to eliminate the threats to public health, biodiversity, and the environment. PFAS, as a class, are of particular concern as these endocrine-disrupting chemicals have become omnipresent and are found not only in pesticides but also in plastic containers, non-stick cookware, cleaning/personal care products, food packaging, and other consumer products. Because of their ubiquitous use, studies report that PFAS compounds are detectable in infants, children, and pregnant women.[15] Furthermore, pregnant women can readily transfer compounds to the developing fetus through the placenta.

It is evident that EPA and other federal regulators are well behind the curve in protecting against the threats posed by PFAS compounds, including PFAS pesticides. Despite evidence on the dangers of PFAS stretching as far back as the 1950s, federal agencies sat on the sidelines, as the plastics industry continued adding the material to new products. The detection of any level of PFAS is cause for concern. As drinking water health advisories issued by EPA show, PFAS levels as low as .02 parts per trillion (ppt) have the potential to cause adverse health effects.[16]

From widespread presence in farm fields and sewage sludge (biosolids) to contaminated water bodies throughout the U.S., PFAS have made their way into the environment and human bodies. Given the recent problems with widespread contamination of agricultural land with PFAS, EPA should not register a new PFAS pesticide, which would further disperse a persistent compound in the environment and could further threaten farmers' livelihoods and lives. PFAS are even present in remote environments like the Arctic, Antarctica, and Eastern European Tibetan Plateau. The U.S. Centers for Disease Control and Prevention (CDC) determined that almost all Americans have some level of PFAS in their bloodstream which highlights PFAS as a chronic danger to people that demands urgent regulatory restrictions, rather than an expansion of the market.[17]

PFAS contamination is much more pervasive than previously thought, polluting storage and transportation containers, food and water resources, and other chemical products. Not only is the public exposed to such chemicals, but those who work in factories that create products that include PFAS, or workers who use them regularly, have higher cumulative exposures as well. This PFAS contamination problem calls for a comprehensive policy rather than the "whack-a-mole" approach to chasing individual contamination crises after they have occurred and inflicted serious harm to people's health. Given EPA's mandatory duty under the *Food Quality Protection Act* (FQPA) to consider aggregate risk from dietary and non-dietary exposure, the addition of a new PFAS-classified pesticide (isocycloseram) without an aggregate risk assessment—taking into account uncertainties associated with the agency's still limited characterization of exposure and the impact on vulnerable populations—would constitute a violation of law.

The solution lies in organic- and agroecology-based land management

PFAS should be banned from all products, and no new chemicals should be approved for use that fall into this class. Organic agroecology-based agriculture offers a long-term solution to PFAS contamination. Utilizing a holistic strategy, such as organic land management under the Organic Foods Production Act (OFPA), the government must consider "cradle-to-grave" impacts—from production through use to disposal—and require that systems be put in place to eliminate the need for use of synthetic materials. In this context, the goal is to eliminate the use of petrochemical substances that are contributing to daily health threats, biodiversity collapse, and the climate emergency. Under OFPA, organic producers are prohibited from using synthetic

inputs unless found by the National Organic Standards Board (NOSB) that their use: "(i) would not be harmful to human health or the environment; (ii) is necessary to the production or handling of the agricultural product because of the unavailability of wholly natural substitute products; and (iii) is consistent with organic farming and handling." Under this standard, petrochemical pesticides and fertilizers, as well as biosolids often contaminated with PFAS, have not been allowed.[18]

As the only agricultural system with a requirement for a farm plan, inspections, and certification for compliance with standards, and rigorous public oversight, organic farming promotes sustainable, cost competitive, and profitable practices that enhance soil health and biodiversity. Agroecology is also a science-based approach to farming that integrates local and Indigenous knowledge and provides a set of ecology-based solutions that do not use pesticides and are economically viable for farmers.

Organic and agroecology-based farming are successfully mitigating the escalating public health, environmental, and climate crises, while EPA inaction on identifying, remediating, and preventing PFAS contamination throughout the country contributes to a growing problem.

We urge the agency to not register any products containing isocycloseram, or any other pesticides that are classified as PFAS, based on the unreasonable risks to health and the environment and the availability of alternative practices.

Thank you for your consideration of our comments.

Respectfully,

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Alternatives to Pesticides; Steve Ellis, Pollinator Stewardship Council; Tamela Trussell, Move Past Plastic (MPP); Thomas Fox, Center for Environmental Health

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[2] Wang, Z. *et al*. (2021) A New OECD Definition for Per- and Polyfluoroalkyl Substances, *Environmental Science & Technology*. Available at: https://pubs.acs.org/doi/10.1021/acs.est.1c06896.

[3] United States Environmental Protection Agency (2025). Isocycloseram. Drinking Water Exposure Assessment for the New Active Ingredient Isocycloseram. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0017.

[4] United States Environmental Protection Agency (2025). Isocycloseram. Report of the Residues of Concern Knowledgebase Subcommittee (ROCKS). Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0011.

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[7] United States Environmental Protection Agency (2025). Isocycloseram Technical Master Label. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0022.

[8] United States Environmental Protection Agency (2025). Memorandum Supporting Proposed Decision to Approve Registration for the New Active Ingredient of Isocycloseram. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0007.

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[10] United States Environmental Protection Agency (2025). Isocycloseram Alternate Brand Name: Equento 400FS A22725 ST - Master Label. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0027.

[11] United States Environmental Protection Agency (2025). Isocycloseram. Human Health Risk Assessment for the Section 3 Registration of the New Active Ingredient Isocycloseram on Treated Seeds, Agricultural Field Crops, Indoor/Outdoor Residential Areas, Residential/Commercial Turf, Greenhouse, Commercial/Industrial Areas, Industrial Structures, and Agricultural Structures. Available at: https://www.regulations.gov/document/EPA-HQ-OPP-2021-0641-0015.

[12] United States Environmental Protection Agency, Office of Water (2018). 2018 Edition of the Drinking Water Standards and Health Advisories Tables. Available at: https://www.epa.gov/system/files/documents/2022-01/dwtable2018.pdf.

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