OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

MEMORANDUM

DATE: June 17, 2024

SUBJECT: **SAFLUFENACIL.** Occupational and Residential Exposure Assessment for Proposed New and Amended Uses on Mint (Peppermint and Spearmint) and Crop Group Conversions and Expansions.

PC Code: 118203
CAS No.: 372137-35-4
Petition No.: 2E9045
Risk Assessment Type: Occupational/Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

Task Group No.: 00484712
Parent Case No.: 00478596
Registration No.: 7969-275, 7969-276, 7969-278
Regulatory Action: Section 3 Registration

Reg. Review Case No.: 7277
40 CFR: §180.649

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The conclusions conveyed in this assessment were developed in full compliance with *EPA Scientific Integrity Policy for Transparent and Objective Science*, and EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions.* The full text of *EPA Scientific Integrity Policy for Transparent and Objective Science*, as updated and approved by the Scientific Integrity Committee and EPA Science Advisor can be found here: https://www.epa.gov/system/files/documents/2023-12/scientific_integrity_policy_2012_accessible.pdf. The full text of the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions* can be found here: https://www.epa.gov/scientific-integrity/approaches-expressing-and-resolving-differing-scientific-opinions.

Introduction

The Registration Division (RD) has requested that the Health Effects Division (HED) conduct an exposure and risk assessment for a proposed new use of saflufenacil on mint (fresh leaves and mint, dried leaves) (peppermint and spearmint); and crop group expansions for Citrus fruit (Crop Group 10-10), Pome fruit (Crop Group 11-10), Stone fruit (Crop Group 12-12), and Tree nuts (Crop Group 14-12). For the crops associated with the crop group expansions, no amendments to the registered use patterns [i.e., maximum use rates, retreatment intervals (RTIs), pre-harvest intervals (PHIs), use of adjuvants, etc.] have been proposed. Therefore, an occupational exposure assessment for these uses was not needed as the previous assessments for these uses are protective.

It is HED policy to use the best available data to assess exposure. Several sources of generic data were used in this assessment as surrogate data in the absence of chemical-specific data, including studies from the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Agricultural Handler Exposure Task Force (AHETF) database; and other registrant-submitted exposure monitoring studies (MRID 44339801). Some of these data are proprietary, and subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

Note: This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on 11/30/2023.

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1.0 Executive Summary

Saflufenacil is a broad-spectrum herbicide in mode-of-action Group 14 (cell membrane disruptors). It acts through the inhibition of protoporphyrinogen oxidase (PPO), resulting in cell membrane damage and subsequent plant death. Saflufenacil is currently registered in the U.S. for use on several raw agricultural commodities including legume vegetables, citrus fruit, pome fruit, stone fruit, tree nuts, cereal grains, cotton, corn, oilseeds, grapes, grass forage/hay/grass grown for seed, olives, soybean, pomegranate, caneberry, fig, and chia.

Proposed Use Profile

Interregional Research Project No. 4 (IR-4), in cooperation with the registrant, Bayer Corporation, has submitted a request for Section 3 registrations for proposed new uses on mint and crop group expansions in Citrus fruit (Crop Group 10-10), Pome fruit (Crop Group 11-10), Stone fruit (Crop Group 12-12), and Tree nuts (Crop Group 14-12). There are two end-use products that are being proposed for new saflufenacil uses. The end-use product, Sharpen® Powered by Kixor® Herbicide (EPA Reg. No. 7969-278), is formulated as a water based suspension concentrate (SC) containing 29.74% ai (2.85 lb ai/gallon of product). The proposed mint use is as a broadcast burndown spray to emerged broadleaf weeds in the dormant season (i.e., when mint is not actively growing in the fall (postharvest) or during winter dormancy) at a maximum application rate of 2.0 oz/A (0.044 lb ai/A), via aerial and groundboom equipment. Separate sequential applications may be made within the dormant season burndown applications by at least 14 days. The proposed mint use does not allow for application via chemigation.

The end-use product, Treevix® Powered by Kixor® Herbicide (EPA Reg. No. 7969-276), is formulated as a water-dispersible granule (WG) containing 70% active ingredient (ai) and proposed for crop group expansions and conversions. Treevix® can only be applied using ground equipment. An occupational exposure assessment for the crop group/subgroups associated with the newly proposed crop group conversions was conducted previously (A. Nowotarski, D379647, 27-JUL-2010 and C. Severini, D456302, 07-AUG-2020). The most recent occupational exposure assessment was conducted for a Section 3 registration for uses on field corn commodities, post-harvest, and fallow (L, Venkateshwara, D467656, 05-DEC-2023).

Both labels require handlers to wear “baseline” attire (i.e., long-sleeved shirt, long pants, shoes and socks), as well as personal protective equipment (PPE) including protective eyewear, and chemical resistant gloves. The restricted entry interval (REI) is 12 hours for the proposed uses. There are currently no registered or proposed residential uses or use sites.

Based on the proposed use pattern, it has been determined that the potential exposure scenarios that will need to be assessed include short- and intermediate-term occupational exposures (handler and post-application).

Exposure Profile

Based on the proposed uses of saflufenacil, it is expected that short- and intermediate-term dermal and inhalation occupational handler and occupational post-application exposures will occur. Chronic exposure is not expected for the proposed use patterns. There are currently no registered or proposed uses in residential settings that would result in residential handler or post-application exposure;

however, there is the potential for non-occupational exposure (dermal and incidental oral) as a result of spray drift.

Hazard Characterization

For all occupational and non-occupational risks, the point of departure (POD) for short- and intermediate-term dermal and inhalation exposure/risk assessment is a no-observed adverse-effect level (NOAEL) of 5 mg/kg/day based on decreased fetal body weights and increased skeletal variations at the lowest-observed adverse-effect level (LOAEL) of 20 mg/kg/day in the developmental study in rats. Since an oral study was used for the dermal POD, a dermal absorption factor (DAF) of 6%, derived from a dermal penetration study (MRID 47128214), was used for the dermal risk assessment. Saflufenacil was classified as "not likely to be carcinogenic to humans" based on the lack of tumors in the mouse and rat carcinogenicity studies and lack of mutagenicity. The total uncertainty factor (UF) that was applied to occupational and non-occupational risk assessments is 100 for short- and intermediate-term risks (10x interspecies factor, 10x intraspecies factor). Since the POD for the dermal and inhalation routes of exposure are based on the same effect, the exposures from these routes can be combined to estimate total risk. Furthermore, the short- and intermediate-term dermal and inhalation levels of concern (LOCs) are the same (LOC = 100).

Residential Exposure and Risk

There are currently no registered or proposed residential uses or use sites for saflufenacil. As such, no residential handler or post-application exposures/risks were assessed.

Occupational Exposure and Risk

Short- and intermediate-term occupational handler inhalation and dermal risk estimates are not of concern. Combined dermal and inhalation margins of exposure (MOEs) range from 2,600 to 50,000 (LOC = 100) with baseline attire and label-required baseline attire and PPE (i.e., protective gloves, protective eyewear and no respirator).

A quantitative post-application dermal exposure assessment was not conducted for the proposed use on mint since the proposed use (see label Sharpen® (EPA Reg. No. 7969-278)), is a broadcast burndown spray to emerged broadleaf weeds in the dormant season (i.e., when mint is not actively growing in the fall (postharvest) or during winter dormancy). The crop conversions and expansion use proposed in the label Treevix® (EPA Reg. No. 7969-276) indicate the application should be directed at the base of the tree trunks; therefore, HED does not expect that post-application dermal exposure will occur. The proposed labels indicate that crop injury will result if the products are applied postemergent (over the top) to any crop.

The REI is based on the acute toxicity of saflufenacil technical material. Saflufenacil is classified as Toxicity Category III for acute oral and acute dermal toxicity. It is classified as Toxicity Category IV for acute inhalation toxicity, acute eye irritation and primary skin irritation. It is not a dermal sensitizer. Therefore, the acute toxicity categories for this chemical require a 12 hour REI under 40 CFR 156.208 (c) (2) (iii). The 12-hour REI, which currently appears on the labels, is adequate for the proposed uses.

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for saflufenacil at this time. If new policies or

procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for saflufenacil.

Human Studies Review

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1, the AHETF database, the ARTF database, and other registrant-submitted exposure monitoring studies (44339801) are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[1].

2.0 Risk Assessment Conclusions and Recommendations

2.1 Summary of Risk Estimates

All occupational handler scenarios for the proposed uses resulted in combined dermal and inhalation risk estimates that are not of concern with baseline attire and label-specified PPE (i.e., single layer, gloves/no respirator). Combined MOEs range from 2,600 to 50,000 (LOC = 100).

2.2 Label Recommendations

Note on mixing/loading liquid formulation scenarios: A 2019 study by the AHETF, a consortium of pesticide manufacturing companies, measured dermal and inhalation exposure for workers who loaded liquid pesticides using closed loading systems such as gravity feed, container breach, and suction/extraction systems. As a result of the review and acceptance of that data, labels for liquid pesticide products for which suction/extraction systems are applicable should instruct users to rinse extraction probes within the pesticide container prior to removal of the probes. These instructions will ensure that users of suction/extraction systems do not remove and handle chemical extraction probes still coated with the concentrated liquid formulation.

2.3 Data Deficiencies and Requirements

None.

3.0 Hazard Characterization

Acute Toxicity

Saflufenacil is classified as Toxicity Category III for acute oral and acute dermal toxicity. It is classified as Toxicity Category IV for acute inhalation, acute eye irritation and acute dermal irritation. It is not a dermal sensitizer. Table 3.1 presents a summary of the acute toxicity information for saflufenacil:

[1] Available online: Occupational Pesticide Handler Exposure Data | US EPA and Occupational Pesticide Post-application Exposure Data | US EPA

Table 3.1. Acute Toxicity Profile – Saflufenacil				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute Oral (rat)	47128101 (93.8% a.i.)	LD_{50} > 2000 mg/kg (F)	III
870.1200	Acute Dermal (rat)	47128102 (93.8% a.i.)	LD_{50} > 2000 mg/kg (M & F)	III
870.1300	Acute Inhalation (rat)	47128103 (93.8% a.i.)	LC_{50} > 5.3 mg/L (M & F)	IV
870.2400	Primary Eye Irritation (rabbit)	47128104 (93.9% a.i.)	Minimally irritating	IV
		47128105 (93.8% a.i.)	Minimally irritating	IV
870.2500	Primary Skin Irritation (rabbit)	47128106 (93.9% a.i.)	Non-irritating	IV
870.2600	Dermal Sensitization (guinea pig)	47128107 (93.8% a.i.)	Not a dermal sensitizer (Maximization)	N/A

Subchronic and chronic toxicity studies for saflufenacil in rats, mice, and dogs identified the hematopoietic system as the primary systemic target. Decreased hematological parameters were seen at about the same dose level across species, except dogs, where the effects were seen at a slightly higher dose. These effects occurred around the same dose level from short- through long-term exposures without increasing in severity. Effects were also seen in the liver in mice, the spleen in rats, and in both these organs in dogs. These effects also occurred around the same dose level from short- through long-term exposures without increasing in severity.

Increased fetal susceptibility was observed in the developmental toxicity studies in the rat and rabbit and in the 2-generation reproduction study in the rat. Developmental effects such as decreased fetal body weights and increased skeletal variations occurred at doses that were not maternally toxic in the developmental study in rats, indicating increased quantitative susceptibility. In rabbits, developmental effects such as increased liver porphyrins were observed at doses that were not maternally toxic, also indicating increased quantitative susceptibility. In the 2-generation reproductive toxicity study in rats, the reported offspring effects were more severe than the maternal effects at the same dose level, indicating evidence for increased qualitative susceptibility.

In a 28-day dermal toxicity study in rats, saflufenacil did not induce any type of dermal or systemic toxicity up to the limit dose of 1,000 mg/kg/day. The Hazard and Science Policy Council (HASPOC) met on July 18, 2013 to discuss the need for a subchronic inhalation toxicity study for saflufenacil (A. Dunbar, TXR 0056720, 02-AUG-2013). Based on a weight-of-evidence approach, the HASPOC recommended that a subchronic inhalation toxicity study is not required for saflufenacil at this time for the following reasons: (1) the physical/chemical properties of saflufenacil including its low volatility (3.4×10^{-17} mmHg, 20°C); (2) its low acute inhalation toxicity (Toxicity Category IV); and (3) the use of an oral POD resulting in inhalation MOEs that are 10x greater than the Agency's LOC (inhalation MOEs > 1,000).

Toxicological PODs Used for Risk Assessment

The toxicity endpoints and the PODs for various exposure scenarios are presented in Table 3.2. For all occupational risks, the POD for short- and intermediate-term dermal and inhalation exposure/risk assessment is a NOAEL of 5 mg/kg/day based on decreased fetal body weights and increased skeletal variations at 20 mg/kg/day (LOAEL) in the developmental study in rats. For overall risk, the dermal and inhalation exposures were added together and compared to the same NOAEL. Chronic exposures are not expected.

Table 3.2. Summary of Toxicological Doses and Endpoints for Saflufenacil for Use in Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure (POD)	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Short-Intermediate-Term (1-30 days and 1-6 months, respectively)	NOAEL = 5 mg/kg/day	UF_A = 10X UF_H = 10X *Dermal absorption Factor = 6%*	Occupational LOC for MOE = 100	Prenatal developmental in (rat) **Developmental NOAEL**= 5 mg/kg/day LOAEL = 20 mg/kg/day based on based on decreased fetal body weights and increase skeletal variations.
Inhalation Short-Intermediate-Term (1-30 days and 1-6 months, respectively)	NOAEL = 5 mg/kg/day	UF_A = 10X UF_H = 10X *Inhalation-absorption assumed equivalent to oral*	Occupational LOC for MOE = 100	Prenatal developmental in (rat) **Developmental NOAEL**= 5 mg/kg/day LOAEL = 20 mg/kg/day based on based on decreased fetal body weights and increase skeletal variations.
Cancer (oral, dermal, inhalation)	Classification: Classification: Not carcinogenic based on the lack of tumors in the mouse and rat carcinogenicity studies and lack of mutagenicity.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (intraspecies). UF_H = potential variation in sensitivity among members of the human population (interspecies). MOE = margin of exposure. LOC = level of concern.

Absorption

A DAF of 6% was estimated for saflufenacil based on the highest degree of skin penetration at the lowest dose tested in a rat dermal absorption study. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure.

Body Weight

Since the dermal and inhalation PODs are based on female specific, developmental, and/or fetal effects, the adult body weight appropriate for dermal and inhalation assessments is 69 kg.

4.0 Use Profile

Saflufenacil is currently registered for use on legume vegetables, citrus fruit, pome fruit, stone fruit, tree nuts, cereal grains, corn, cotton, grapes, grass forage/hay/grass grown for seed, olives, soybean, pomegranate, caneberry, fig, and chia. IR-4 is proposing new use on mint and crop group expansions for Citrus fruit (Crop Group 10-10), Pome fruit (Crop Group 11-10), Stone fruit (Crop Group 12-12), and Tree nuts (Crop Group 14-12). For the crops associated with the crop group expansions, no amendments to the use patterns [i.e., maximum use rates, retreatment intervals (RTIs), PHIs, use of

adjuvants, etc.] have been proposed. Therefore, an occupational exposure assessment for these uses was not needed.

The maximum single application rate is 0.044 lb ai/A, and a summary of directions for the proposed mint use is detailed below in Table 4.1.

Table 3.3.2. Summary of Directions for Use of Saflufenacil.

Formulation	Applic. Timing, Type, and Equip.	Max Single App. Rate (lb ai/A)	Max. # Apps per year	Max Seasonal App. Rate (lb ai/A)	RTI (days)	PHI (days)	Use Directions and Limitations	PPE
Mint (New Use – Post-emergence)								
Sharpen® powered by Kixor® Herbicide. (7969-278) SC	Broadcast spray Groundboom sprayer, Fixed wing, Helicopter	0.044	2	0.044	-	No required (PHI)	• Broadcast burndown spray to emerged broadleaf weeds in the dormant season (i.e., when mint is not actively growing in the fall (postharvest) or during winter dormancy). • Separate sequential applications may be made within the dormant season if the maximum cumulative amount does not exceed 2.0 fl ozs/A. Separate sequential dormant season burndown applications by at least 14 days. • Do not apply to mint that has broken dormancy. Do apply to mint in the first year of growth and establishment. Do not apply to mint stands that have been weakened by age, disease, cold weather, excessive moisture, or other factors that reduce crop vigor. • Do not apply by chemigation. • For use in Idaho, Indiana, Michigan, Montana, Oregon, Utah, Washington, and Wisconsin.	• Long-sleeved shirt, long pants • Shoes plus socks • Waterproof glove • Protective eyewear.

PHI = preharvest interval; RTI = retreatment interval; SC = Suspension Concentrate.

5.0 Residential Exposure and Risk Estimates

There are no residential uses proposed or currently registered for saflufenacil. As such, no residential handler and post-application exposure/risk was assessed.

6.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Spray drift is a potential source of exposure to individuals who are located in close proximity to pesticide applications. This is particularly the case with aerial application, which tends to have the highest amount of drift as evaluated, but spray drift can also be a potential source of exposure from the ground application methods. The Agency has developed best spray drift management practices

with input from the Spray Drift Task Force[2], EPA Regional Offices, and State Lead Agencies for pesticide regulation as well as other parties (see the Agency's Spray Drift website for more information).[3] The Agency has also prepared a draft document on how to appropriately consider spray drift as a potential source of exposure in risk assessments for pesticides. The approach is outlined in the revised 2013 *Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift*, which can be found at Regulations.gov in docket identification number EPA-HQ-OPP-2013-0676. The potential for spray drift from saflufenacil uses will be evaluated during the ongoing Registration Review process to ensure that all uses for that pesticide will be considered concurrently.

7.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from FIFRA Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010[4]. The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (*Human Health Bystander Screening Level Analysis: Volatilization of Conventional Pesticides*[5]).

During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for saflufenacil.

8.0 Occupational Exposure and Risk Estimates

8.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed uses.

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[2] This task force was organized in 1990, pursuant to the provisions of FIFRA section 3(c)(2)(B)(ii). It was comprised of pesticide registrants and those applying for registration of pesticide products to give them the option of fulfilling spray drift data requirements by participating in the task force, which would share the cost of developing a generic spray drift database expected to be capable of satisfying spray drift data requirements for virtually all pesticide product registrations in the United States and Canada. Available online: PRN 90-3: Announcing the Formation of an Industry-Wide Spray Drift Task Force | US EPA

[3] EPA's webpage is available online: Reducing Pesticide Drift | US EPA. It contains extensive information about EPA's efforts to reduce spray drift as well as additional materials and links to educational materials that provide information about practices for reducing spray drift.

[4] Available online: A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding Field Volatilization of Conventional Pesticides | US EPA ARCHIVE DOCUMENT

[5] Available online: Regulations.gov

The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios presented in Table 8.1.

Occupational Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor are detailed below on an individual basis.

Application Rate: The application rates used in this assessment is 0.044 lb ai/A and is fully detailed in Table 4.1.

Unit Exposures:
It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in: the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[6]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[7], which, along with additional information on seed treatment exposure assessment, can be found at the Agency website

Area Treated or Amount Handled:
The inputs for area treated/amount handled were based on information in ExpoSAC Policy 9.2.

Exposure Duration:
HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (e.g., completing multiple applications for multiple clients within a region).

For saflufenacil, based on the proposed uses, short- and intermediate-term exposures are expected; however, the PODs for short- and intermediate-term exposures are the same therefore, short-term exposure and risk estimates are protective of longer-term durations.

Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated for various levels of PPE. Results are presented for label PPE defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, protective gloves, and no respirator. Note, the aerial applicator scenario below the aerial results also include engineering controls (EC/G and EC/No-

[6] Available online: Occupational Pesticide Handler Unit Exposure Surrogate Reference Table 2021 (epa.gov)
[7] Available online: Occupational Pesticide Handler Exposure Data | US EPA

R). The saflufenacil proposed product labels direct mixers, loaders, applicators and other handlers to wear**:**

- Label 7969-276: Protective eyewear (face shield, goggles, or safety glasses), long-sleeved shirt and long pants, shoes plus socks, and chemical-resistant gloves
- Label 7969-278: Protective eyewear (face shield, goggles, or safety glasses), long-sleeved shirt and long pants, shoes plus socks, and waterproof gloves

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix A.

Combining Exposures/Risk Estimates:

Dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were similar. Dermal and inhalation risk estimates were combined using the following formula:

Total MOE = Point of Departure (mg/kg/day) ÷ Combined dermal + inhalation dose (mg/kg/day)

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

The combined dermal and inhalation occupational risk estimate MOEs range from 2,600 to 50,000 with baseline attire and label PPE (long-sleeved shirt, long pants, shoes and socks, protective eyewear, and chemical-resistant gloves). All MOEs are ≥ LOC of 100 and are not of concern. A summary of occupational handler exposure risk estimates can be found in Table 8.1.

Note on flagger scenarios: The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for human flaggers where appropriate, agricultural aviation has changed dramatically over the past two decades. According the 2012 National Agricultural Aviation Association (NAAA) survey of their membership, the use of GPS for swath guidance in agricultural aviation has grown steadily from the mid 1990's. Over the same time period, the use of human flaggers for aerial pesticide applications has decreased steadily from ~15% in the late 1990's to only 1% in the most recent (2012) NAAA survey. The Agency will continue to monitor all available information sources to best assess and characterize the exposure potential for human flaggers in agricultural aerial applications.

Note on aerial applicator scenario: HED has no data to assess exposures to pilots using open cockpits. The only data available is for exposure during aerial applications (covering both airplanes and helicopters) of liquid formulations to pilots in enclosed cockpits (data from AHETF) and of granule formulations in enclosed cockpits (data from PHED). Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); use of the data in this fashion is consistent with the Agency's Worker Protection Standard (WPS) stipulations for engineering controls, which says label-required PPE for applicators can be reduced when using an enclosed cockpit (40 CFR 170.607(f)(3)) as well as a provision regarding use of gloves for aerial applications (40 CFR 170.607(f)(1)), which says pilots are not required to wear

protective gloves for the duration of the application, unless gloves are otherwise required for pilots on the pesticide product labeling. With this level of protection, there are no risk estimates of concern for applicators.

Note on mixing/loading liquid formulation scenarios: A 2019 study by the AHETF measured dermal and inhalation exposure for workers who loaded liquid pesticides using closed systems such as gravity feed, container breach, and suction/extraction systems. After analyzing the exposure monitoring data, the AHETF observed that exposures were higher than expected and subsequently identified that, when using suction/extraction systems, removing and handling chemical extraction probes without rinsing them prior to removal from the pesticide container had the potential to result in high exposures via direct exposure to the liquid concentrate. The AHETF therefore submitted to the Agency a dataset that excludes monitoring of those workers who handled unrinsed chemical extraction probes and recommended that the Agency take additional regulatory actions to ensure workers do not remove and handle chemical extraction probes still coated with the concentrated liquid formulation.

The Agency agreed with the AHETF proposal, recognizing that handling of unrinsed chemical extraction probes is inconsistent with the exposure reduction principles of closed systems. Closed loading systems are an engineering control designed to prevent direct contact between users and the pesticide formulation, thereby reducing exposures. According to EPA's Worker Protection Standard (WPS), a closed system must remove the pesticide from its original container and transfer the pesticide product through connecting hoses, pipes and couplings that are sufficiently tight to prevent exposure of handlers to the pesticide product, except for the negligible escape associated with normal operation of the system [40 CFR § 170.607(d)(2)(i)]. However, in addition to considerations regarding closed systems, given the high exposure potential from this activity, the Agency is requiring revisions to applicable product label instructions to restrict handling un-rinsed extraction probes and conducting stakeholder outreach and revising worker training modules to ensure that users of suction/extraction systems rinse the chemical extraction probes within the pesticide container prior to their removal so that they are not exposed to the concentrated liquid formulation.

Table 8.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Saflufenacil.

Exposure Scenario	Crop or Target	Dermal Unit Exposure[1] (µg/lb ai)	Level of PPE or Engineering control	Inhalation Unit Exposure[1] (µg/lb ai)	Level of PPE or Engineering control	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Dermal		Inhalation		Total
								Dose[4] (mg/kg/day)	MOE[5] (LOC=100)	Dose[6] (mg/kg/day)	MOE[7] (LOC=100)	MOE[8] (LOC=100)
Mixer/Loader												
Liquid, Aerial, Broadcast	Field crop, high-acreage	37.6	SL/G	0.219	No-R	0.044 lb ai/acre	1200 acres	0.00173	2900	0.000168	30000	2600
Liquid, Groundboom, Broadcast	Field crop, high-acreage	37.6	SL/G	0.219	No-R	0.044 lb ai/acre	200 acres	0.000288	17000	0.000028	180000	16000
Applicator												
Spray (all starting formulations), Aerial, Broadcast	Field crop, high-acreage	2.08	EC/G	0.0049	EC/No-R	0.044 lb ai/acre	1200 acres	0.0000957	52000	0.00000375	1300000	50000
Spray (all starting formulations), Groundboom, Broadcast	Field crop, high-acreage	16.1	SL/G	0.34	No-R	0.044 lb ai/acre	200 acres	0.000123	41000	0.0000433	120000	31000
Flagger												
Spray (all starting formulations), Aerial, Broadcast	Field crop, high-acreage	12	SL/G	0.202	No-R	0.044 lb ai/acre	350 acres	0.000161	31000	0.0000451	110000	24000

1 Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data); Level of PPE: SL/G = single layer, gloves; EC = engineering controls; No-R = no respirator.

2 Based on proposed label (Reg. No. 7969-278).

3 Exposure Science Advisory Council Policy #9.2.

4 Dermal Dose = Dermal Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A or gal/day) × DAF (6%) ÷ BW (69 kg).

5 Dermal MOE = Dermal NOAEL (5 mg/kg/day) ÷ Dermal Dose (mg/kg/day).

6 Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A or gal/day) ÷ BW (69 kg).

7 Inhalation MOE = Inhalation NOAEL (5 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

8 Total MOE = NOAEL (5 mg/kg/day) ÷ Dermal Dose + Inhalation Dose.

8.2 Occupational Post-application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

8.2.1 Occupational Post-application Inhalation Exposure/Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from FIFRA Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010[8]. The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (*Human Health Bystander Screening Level Analysis: Volatilization of Conventional Pesticides*[9]). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for saflufenacil.

Although a quantitative occupational post-application inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than post-application exposure, and all of the occupational handler scenarios resulted in inhalation risk estimates that were not of concern at baseline (i.e., all inhalation MOEs without a respirator ≥ the LOC). Therefore, it is expected that these handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios.

8.2.2 Occupational Post-application Dermal Exposure/Risk Estimates

The end-use product, Sharpen® supplemental label (EPA Reg. No. 7969-278) states for mint, saflufenacil can only be applied to dormant established stands (defined as at least one year after planting) mint, up to two applications can be made per crop season and as a broadcast burndown spray to emerged broadleaf weeks in the dormant season (i.e., when mint is not actively growing in fall (post-harvest) or during winter dormancy. Note, for the proposed uses for saflufenacil on mint, there is no required PHI interval between a dormant application and the harvest of mint. HED does not expect post-application dermal exposure will occur. HED does not expect post-application dermal exposure will occur.

[8] Available online: A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding Field Volatilization of Conventional Pesticides | US EPA ARCHIVE DOCUMENT

[9] Available online: Regulations.gov

The EP, Treevix® (EPA Reg. No. 7969-276) is proposed for several crop group expansions: Citrus fruit (Crop Group 10-10), Pome fruit (Crop Group 11-10), Stone fruit (Crop Group 12-12), Tree nuts (Crop Group 14-12). The label states the application should be directed at the base of the tree trunks; therefore, HED does not expect that post-application dermal exposure will occur. The label also indicates that crop injury will result if the products are applied post emergent (over the top) to any crop.

Restricted Entry Interval

Saflufenacil is classified as Toxicity Category III via the dermal route and Toxicity Category IV for skin irritation potential. It is not a skin sensitizer. Short- and intermediate-term post-application risk estimates were not a concern on day 0 (12 hours following application) for all post-application activities. Under 40 CFR 156.208 (c) (2), is classified as Acute III or IV for acute dermal, eye irritation and primary skin irritation are assigned a 12-hour REI. Therefore, the [156 subpart K] Worker Protection Statement interim REI of 12 hours is adequate to protect agricultural workers from post-application exposures to saflufenacil. HED would recommend a REI of 12 hours. This is the REI listed on the proposed labels and is considered protective of post-application exposure.

Appendix A. Summary of Occupational and Residential Non-cancer Algorithms

Occupational Non-cancer Handler Algorithms

Potential daily exposures for occupational handlers are calculated using the following formulas:

$$E = UE * AR * A * 0.001\ mg/\mu g$$

where:

E = exposure (mg ai/day),
UE = unit exposure (µg ai/lb ai),
AR = maximum application rate according to proposed label (lb ai A or lb ai/gal), and
A = area treated or amount handled (e.g., A/day, gal/day).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day),
E = exposure (mg ai/day),
AF = absorption factor (dermal and/or inhalation), and
BW = body weight (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE = margin of exposure: value used by HED to represent risk estimates (unitless),
POD = point of departure (mg/kg/day), and
ADD = average daily dose absorbed in a given scenario (mg ai/kg/day).