OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

MEMORANDUM

DATE: July 3, 2024

SUBJECT: **Flazasulfuron.** Occupational and Residential Exposure Assessment for the Proposed Use on Avocados.

PC Code: 119011
CAS No.: 104040-78-0
Petition No.: 3F9055
Risk Assessment Type: Occupational/Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

Task Group No.: 00484549
Parent Case No.: 00477952
Registration No.: 71512-18
Regulatory Action: Section 3
Case No.: NA
40 CFR: §180.655

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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.

The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration Division (RD) of OPP has requested that HED evaluate hazard and exposure data and conduct occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the proposed uses of flazasulfuron in/on avocado. A summary of the findings and an assessment of human health risk resulting from the proposed uses of flazasulfuron are provided in this document.

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 Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); and 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 11/09/2023

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1.0 Executive Summary

Flazasulfuron (*N*-[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(trifluoromethyl)-2-pyridinesulfonamide) is an herbicide which acts by inhibiting the acetolactate synthase (ALS) biochemical process for control of certain broadleaf weeds and grasses. It is currently registered for use on residential turf, golf courses, sod farms, athletic fields, commercial lawns, Christmas tree farms, and industrial vegetation management in non-agricultural areas. Additionally, flazasulfuron is used on the following agricultural crops: conifer trees, citrus, grapes, tree nuts, olives, and sugarcane.

Proposed Use Profile

ISK Biosciences Corporation has requested avocado to be added to the end-use product (EP) ISK Flazasulfuron Herbicide label (EPA Reg. No. 71512-18). ISK Flazasulfuron Herbicide is a water dispersible granule (WDG) formulation containing 25.0% active ingredient (ai) (0.25 lb ai per lb of product). The single use maximum application rate for avocado is 0.045 lb ai/A, with a single maximum seasonal rate of 0.09 lb ai/A/year. Applications may be made both pre- and post-emergent via ground or handheld equipment only; application by aerial and chemigation equipment are prohibited. The pre-harvest interval (PHI) for avocado is 0 days, and the minimum retreatment interval (RTI) is 90 days. Applicators and other handlers are required to wear "baseline attire" (i.e., long-sleeved shirt, long pants, shoes, and socks) with additional personal protective equipment (PPE) consisting of waterproof gloves and protective eyewear. The restricted-entry interval (REI) specified on the proposed product label is 12 hours.

Exposure Profile

Based on the proposed uses of flazasulfuron on avocados, occupational handler exposure is expected to occur for short- (1 to 30 days) and intermediate-term (1 to 6 months) durations during mixing, loading, applying, and other handling activities. Long-term exposure is not expected for the proposed use patterns. Additionally, there is a potential for short- and intermediate-term occupational exposure from re-entry during post-application activities. Residential exposures are not expected from the proposed use; however, non-occupational exposure resulting from spray drift from agricultural applications onto residential areas may occur. Exposures from spray drift are expected to be short-term only.

Hazard Characterization

The flazasulfuron toxicity database is considered complete. An incidental oral and short- and intermediate-term inhalation no observed adverse effect level (NOAEL) of 2 mg/kg/day was selected based on systemic effects observed at the lowest observable adverse effect level (LOAEL) of 10 mg/kg/day from a 90-day oral toxicity study in dogs. The Hazard and Science Policy Council (HASPOC) recommended to waive the requirement for a subchronic inhalation toxicity study (K. Rury, TXR 0056483, 10/04/2012). 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. No short- or intermediate-term dermal hazard was identified. Since the inhalation endpoint is not based on developmental effects, the average body weight of an adult (80 kg) was used in the exposure assessments. Flazasulfuron has low acute toxicity via dermal (Toxicity Category III), and oral and inhalation (Toxicity Category IV) routes of exposure. Flazasulfuron is not a skin irritant or a dermal sensitizer, but it is a moderate eye irritant (Toxicity Category III). The cancer classification for flazasulfuron is "not likely to be carcinogenic to humans."

The flazasulfuron risk assessment team evaluated the quality of the toxicity and exposure data and recommended that the Food Quality Protection Act (FQPA) Safety Factor (SF) be reduced to 1X. Therefore, the level of concern (LOC) is equal to a margin of exposure (MOE) of 100 (10X factor to account for interspecies extrapolation, 10X factor to account for intraspecies sensitivity, and 1X for FQPA SF).

Residential Exposure Assessment and Risk Estimates

There are no residential exposures expected from the proposed use of flazasulfuron on avocado. However, there are existing residential turf exposures that have been previously assessed using current data and assumptions (C. Walls, D399890, 10/09/2012). All residential risk estimates previously assessed resulted in no risks of concern and are presented herein for use in the aggregate risk assessment for flazasulfuron.

Occupational Handler Exposures and Risk Estimates

Although dermal exposure can occur, a dermal point of departure (POD) was not selected for flazasulfuron, therefore, the occupational handler assessment includes only inhalation exposures. There are no risk estimates of concern for occupational handler inhalation exposure (i.e., margins of exposure (MOEs) ≥ the level of concern (LOC) of 100) with baseline attire only (i.e., long-sleeved shirt, long pants, shoes, socks, and no respirator). The short-term occupational inhalation MOEs range from 6,200 to 520,000.

Summary of Occupational Post application Exposure and Risk Estimates

Since no hazard was identified for the dermal route of exposure, dermal post-application exposures were not quantitatively assessed.

Based on the Agency's current practices, a quantitative non-cancer post-application inhalation exposure assessment was not performed for flazasulfuron at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative post-application inhalation exposure assessment for flazasulfuron.

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, and other registrant-submitted exposure monitoring studies (MRID 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

[1] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

2.1 Summary of Risk Estimates

There are no occupational handler inhalation risk estimates of concern for the proposed new use on avocado. Occupational inhalation MOEs range from 6,200 to 520,000 using baseline attire (i.e., no respirator; LOC = 100).

2.2 Label Recommendations

None.

3.0 Hazard Characterization

The hazard profile for flazasulfuron has not changed since the previous risk assessment (C. Walls, D417418, 01/31/2014). The hazard database for flazasulfuron is well-characterized and complete.

A short-term incidental oral and short- and intermediate-term inhalation NOAEL of 2 mg/kg/day was selected as the point of departure (POD) from the oral subchronic toxicity study in dogs based on changes in the liver (increase in: deposition of brown pigments, glutamic pyruvic transaminase, creatine phosphokinase, inflammatory cell infiltration, and microgranulomas) at the LOAEL of 10 mg/kg/day. The HASPOC has recommended to waive the requirement for a subchronic inhalation toxicity study (K. Rury, TXR 0056483, 10/04/2012). No dermal hazard was identified because no effects were seen up to the limit dose (1,000 mg/kg/day) in a 21-day dermal toxicity study. Furthermore, there were no developmental or reproductive effects observed in the database. The FQPA SF has been reduced to 1X because the toxicity database is complete, there is no concern for quantitative or qualitative susceptibility in offspring, there are no neurotoxicity concerns, and there are no residual uncertainties regarding exposure.

HED's LOC for the MOE is defined by the uncertainty factors that are applied to the assessment. HED applies a 10X factor to account for interspecies extrapolation and a 10X factor to account for intraspecies sensitivity. Therefore, the total uncertainty factor that has been applied to the non-cancer risk assessment is equal to an LOC of 100 for occupational and residential exposure. Occupational and residential risks resulting in MOEs greater than or equal to 100 do not exceed HED's LOC.

Flazasulfuron has low acute toxicity via the oral (Tox Category IV), dermal (Tox Category III), and inhalation (Tox Category IV) routes of exposure. It is not irritating to the skin or eyes and is not a sensitizer. The most consistently observed effects of flazasulfuron exposure across species, genders, and treatment durations were kidney and liver toxicity. Subchronic studies indicated decreased body weight gain and slight anemia in rats and liver abnormalities in dogs. The acute toxicity findings for technical flazasulfuron are presented in Table 3.1.

Table 3.1. Acute Toxicity Profile – Flazasulfuron.				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute Oral (rat)	46220908	$LD_{50} \geq 5000$ mg/kg (M & F)	IV
870.1200	Acute Dermal (rat)	46220909	$LD_{50} \geq 2000$ mg/kg (M & F)	III
870.1300	Acute Inhalation (rat)	46220910	$LC_{50} \geq 5.99$ mg/L (M & F)	IV
870.2400	Primary Eye Irritation (rabbit)	46220911	Minimal conjunctivitis through 48 hours. Free by 72 hours.	III
870.2500	Primary Skin Irritation (rabbit)	46220912	No erythema, edema, or dermal effects observed at application site.	IV
870.2600	Dermal Sensitization (guinea pig)	46220913	Not a dermal sensitizer (Buehler Method)	N/A

Applicable toxicological doses and endpoints for use in this risk assessment are presented in Table 3.2.

Table 3.2. Summary of Toxicological Doses and Endpoints for Flazasulfuron for Use in Human Health Risk Assessments.				
Exposure/Scenario	**POD**	**Uncertainty/ FQPA SF**	**LOC for Risk Assessment**	**Study and Toxicological Effects**
Incidental Oral Short-Term (1 - 30 days) Children (1 to <2 years old)	NOAEL = 2 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	LOC for MOE = 100	90-Day oral toxicity in (dog) LOAEL= 10 mg/kg/day based on changes in liver (increase in: deposition of brown pigments, glutamic pyruvic transaminase, creatine phosphokinase, inflammatory cell infiltration, microgranulomas).
Dermal Short-Term (1 - 30 days) Intermediate-Term (1-6 months)	No dermal toxicity was observed in the 21-day dermal toxicity study up to the limit dose. Increased susceptibility was seen in rat developmental studies; however, applying a 20% dermal absorption rate to developmental LOAELs gives estimated dermal equivalent doses well above the limit dose of 1,000 mg/kg/day. Therefore, a dermal risk assessment was not conducted.			
Inhalation Short-Term (1 - 30 days) and Intermediate-Term (1 - 6 months)	NOAEL = 2 mg/kg/day (Inhalation toxicity considered equivalent to oral toxicity.)	UF_A = 10X UF_H = 10X FQPA SF = 1X	LOC for MOE = 100	90-Day oral toxicity in (dog) LOAEL = 10 mg/kg/day based on changes in liver (increase in: deposition of brown pigments, glutamic pyruvic transaminase, creatine phosphokinase, inflammatory cell infiltration, microgranulomas).
Cancer (oral, dermal, inhalation)	**Classification:** Not likely to be carcinogenic to humans			

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 (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern. FPQA SF = Food Quality Protection Act Safety Factor.

Body Weight

The standard body weight for the general population (80 kg) was used for all exposure scenarios covered in this risk assessment since the endpoints selected were not developmental and/or fetal effects.

Absorption

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.

4.0 Use Profile

ISK Biosciences Corporation has requested avocado to be added to EP ISK Flazasulfuron Herbicide label (EPA Reg. No. 71512-18). ISK Flazasulfuron Herbicide is a WDG formulation containing 25.0% ai (0.25 lb ai/lb product). The single use maximum application rate for avocado is 0.045 lb ai/A, with a maximum seasonal rate of 0.09 lb ai/A/year. Applications may be made both pre- and post-emergent via ground or handheld equipment only; application by aerial and chemigation equipment are prohibited. The PHI for avocado is 0 days and the minimum RTI is 90 days. Applicators and other handlers are required to wear "baseline attire" (i.e., long-sleeved shirt, long pants, shoes, and socks) with additional PPE consisting of waterproof gloves and protective eyewear. The REI specified on the product label is 12 hours.

The proposed use of flazasulfuron is summarized in Table 4.1.

Table 4.1. Use Profile for Proposed Flazasulfuron Use.

Applic. Timing, Type, and Equip.	Product, Formulation, [EPA Reg. No.]	Max. Single Applic. Rate lb ai/A (conc. for handheld equipment)	Max. No. Applic. Per Year	Max. Annual Applic. Rate (lb ai/A)	Use Directions and Limitations
Avocado					
Pre-emergent, Post-emergent; Ground, Handheld Equipment	ISK Flazasulfuron Herbicide (0.25 lb ai/lb of product) [71512-18]	0.045 (0.003 lb ai/gal of solution)	2	0.09	Do not apply aerially or through an irrigation system. Do not mechanically incorporate into the soil. Apply using spray volumes of 15 to 50 GPA. 12-hour REI. 90-day RTI. 0-day PHI.

PHI = Pre-harvest interval. REI = Restricted entry interval. GPA = gallons per acre. RTI = Retreatment interval.

5.0 Residential Exposure and Risk Estimates

There are no residential exposures associated with the proposed uses in this action; however, there are residential exposures from existing registered uses on turf that have been previously assessed using current data and assumptions for flazasulfuron (C. Walls, D399890, 10/09/2012). Risk estimates have been presented for the purpose of aggregate assessment; all residential risk estimates are not of concern.

5.1 Residential Risk Estimates for Use in Aggregate Assessment

Table 5.1.1 reflects the residential risk estimates that are recommended for use in the aggregate assessment for flazasulfuron.

- The recommended residential exposure for use in the adult aggregate assessment reflects inhalation exposure from applying water dispersable granules (WDG) to turf via backpack or manually-pressurized handwand.
- The recommended residential exposure for use in the children 1 to <2 years old aggregate assessment reflects hand-to-mouth exposures from post-application exposure to previously treated turf.

Table 5.1.1. Recommendations for the Residential Exposures for the Flazasulfuron Aggregate Assessment.[1]

Lifestage	Handler Exposure (mg/kg/day)[2]		Residential Handler Total Exposure (mg/kg/day)	Residential Handler Total MOE (LOC=100)	Post-application Exposure (mg/kg/day)[3]			Residential Post-application Total Exposure (mg/kg/day)	Residential Post-application MOE (LOC=100)
	Dermal	Inhalation			Dermal	Inhalation	Oral		
Short-Term									
Adult	NA	0.000073	**0.000073**	27,000	NA	NA	N/A	NA	NA
Child	N/A	N/A	N/A	NA	NA	NA	0.00069	**0.00069**	2,900

[1] Bolded risk estimates are recommended for use in the residential exposure portion of the aggregate assessment.

[2] Handler exposure represents high-end handler exposure (i.e., the highest handler exposure of all scenarios assessed).

[3] Post-application exposure represents high-end dermal, inhalation, and/or incidental oral exposure for the relevant exposure duration.

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 https://www.regulations.gov in docket identification number EPA-HQ-OPP-2013-0676. The potential for spray drift from flazasulfuron uses will be evaluated during the ongoing Registration Review process to ensure that all uses for that pesticide will be considered concurrently.

[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. See https://www.epa.gov/pesticide-registration/prn-90-3-announcing-formation-industry-wide-spray-drift-task-force.

[3] EPA's webpage entitled "Reducing Pesticide Drift" is located at http://www2.epa.gov/reducing-pesticide-drift. 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.

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 flazasulfuron.

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.

The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios presented below in 8.1.1.

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 is detailed below on an individual basis.

Application Rate: A summary of the maximum application rate for the proposed use is provided 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 and the AHETF database. 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

[4] Available: http://archive.epa.gov/scipoly/sap/meetings/web/pdf/120309meetingminutes.pdf
[5] Available: https://www.regulations.gov/document/EPA-HQ-OPP-2014-0219-0002

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]

Area Treated or Amount Handled: The inputs for area treated or amount handled are 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 flazasulfuron, based on the proposed use, short- and intermediate-term exposures are expected. Additionally, since the same endpoint and POD were selected for short- and intermediate-term durations, short-term exposure and risk estimates are considered to be protective of intermediate-term exposure and risk.

Personal Protective Equipment: Based on the product label for flazasulfuron, applicators and other handlers must wear baseline attire (i.e., long-sleeve shirts, long pants, socks, shoes, and no respirator) and PPE consisting of waterproof gloves and protective eyewear. Estimates of inhalation exposure were calculated with baseline attire, defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator.

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:

Occupational handler dermal and inhalation exposure is anticipated from the proposed flazasulfuron use; however a dermal endpoint was not selected. Therefore, only inhalation exposures have been quantitatively assessed.

Summary of Occupational Handler Exposure and Risk Estimates

All inhalation MOEs for the occupational handler exposure are greater than the LOC of 100 and therefore are not of concern; inhalation MOEs range from 6,200 to 520,000. Table 8.1.1 summarizes the flazasulfuron occupational handler exposures and risks.

[6] Available: https://www.epa.gov/sites/default/files/2021-05/documents/occupational-pesticide-handler-unit-exposure-surrogate-reference-table-may-2021.pdf

[7] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

Table 8.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Flazasulfuron.						
Exposure Scenario	Crop or Target	Unit Exposure[1] (µg/lb ai)	Max App. Rate[2]	Area Treated or Amount Handled Daily[3]	Inhalation	
		Inhalation [PPE]			Dose (mg/kg/day)[4]	MOE[5] LOC=100
Mixer/Loader						
Dry Flowable, Airblast, Broadcast	Avocado (orchard/vineyard)	8.96 [No-R]	0.045 lb ai/A	40 acres	0.000201	10,000
Dry Flowable, Groundboom, Broadcast						
Applicator						
Spray (all starting formulations), Airblast, Broadcast	Avocado (orchard/vineyard)	4.71 [No-R]	0.045 lb ai/A	40 acres	0.000106	19,000
Spray (all starting formulations), Groundboom, Broadcast		0.34 [No-R]		40 acres	0.00000765	260,000
Mixer/Loader/Applicator						
Dry Flowable, Backpack, Ground/Soil-Directed	Avocado (orchard/vineyard)	2.58 [No-R]	0.003 lb ai/gal	40 gallons solution	0.00000388	520,000
Dry Flowable, Mechanically-pressurized Handgun, Broadcast (foliar) and Ground-Directed	Avocado (orchard/vineyard)	8.68 [No-R]	0.003 lb ai/gal	1,000 gallons solution	0.000325	6,200

[1] Unit Exposures: Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (Occupational Pesticide Handler Unit Exposure Surrogate Reference Table 2021 (epa.gov)); Level of PPE: No-R = no respirator.
[2] Maximum Application Rate: Based on proposed label (see Table 4.1).
[3] Area Treated or Amount Handled: Exposure Science Advisory Council Policy #9.2.
[4] Inhalation Dose: 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 Daily (A or gal/day) ÷ BW (80 kg).
[5] MOE: Inhalation MOE = Inhalation POD (2 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 100.

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 its FIFRA SAP in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis

(https://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). 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 flazasulfuron.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the Agriculture Re-entry Task Force (ARTF). Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the agency's risk assessments.

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. 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

While occupational dermal post-application exposures are anticipated, a dermal endpoint has not been selected for flazasulfuron; therefore, a dermal post-application risk assessment was not conducted.

Restricted Entry Interval

The REI specified on the amended label is based on the acute toxicity of flazasulfuron. Flazasulfuron is classified as Toxicity Category III via the dermal route and Toxicity Category IV for skin irritation potential. It is not a skin sensitizer. Under 40 CFR 156.208 (c) (2) (iii), ai's classified as Acute III or IV for acute dermal, eye irritation and primary skin irrigation 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 flazasulfuron. HED would recommend the REI on the product labels be consistent with the WPS recommendations. This is the REI listed on the proposed label and is considered protective of post-application exposure.

Appendix A. Occupational Handler Exposure Calculations

Occupational Handler Exposure Algorithm

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

$$E=UE * AR * A * 0.001\ mg/ug$$

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).