OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: **July 16, 2024**

SUBJECT: **Ethaboxam.** Occupational and Residential Exposure Assessment for a Proposed Use on Leaf Petiole Vegetable in Greenhouses.

PC Code: 090205
CAS No.: 162650-77-3
Decision No.: 591231
Petition No.: 3E9052
Risk Assessment Type: Occupational/Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

DP Barcode: D468066
Task Group No.: 00620365
Parent Case No.: 00475265
Registration No.: 59639-185, 59639-211
Regulatory Action: Section 3

Reg. Review Case No.: NA
40 CFR: §180.622

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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: EPA's Scientific Integrity Policy. The full text of the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions* can be found here: Approaches for Expressing and Resolving Differing Scientific Opinions | US EPA.

Introduction

The Registration Division (RD) has requested that the Health Effects Division (HED) conduct an exposure and risk assessment for the proposed Section 3 registration of ethaboxam on leaf petiole vegetable (crop subgroup 22b) grown in greenhouses.

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); the Agricultural Handler Exposure Task Force (AHETF) database; and the Agricultural Re-entry Task Force (ARTF) database. 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 11/02/2023.

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1.0 Executive Summary

Ethaboxam (N-(cyano-2-thienylmethyl)-4-ethyl-2-(ethylamino)-5-thiazolecarboxamide) is a thiazole carboxamide fungicide that controls various diseases caused by *Phytophthora*, *Plasmopara*, and *Aphanomyces* species. Ethaboxam is currently registered for use on *Brassica* head and stem vegetables (crop group 5-16), *Brassica* leafy greens (crop subgroup 4-16B), cucurbit vegetables (crop group 9), ginseng, peppers/eggplants (crop subgroup 8-10B), and tuberous and corm vegetables (crop subgroup 1C), as well as a seed treatment on a variety of seeds (i.e., legume vegetables [crop group 6], cereal grains [crop group 15] except rice and wild rice, rapeseed [crop subgroup 20A], sunflower subgroup 20B, and sugar beets, and alfalfa).

Interregional Research Project No. 4 (IR-4) on behalf of the registrant, Valent U.S.A. LLC, is requesting a Section 3 registration for the proposed new use of ethaboxam on leaf petiole vegetable subgroup 22B grown in greenhouses.

Use Profile

The proposed end-use product, V-10208 4 SC Fungicide (EPA Reg. No. 59639-211) is formulated as a suspension concentrate containing 42.5% ethaboxam (4 pounds (lb) active ingredient (ai) per gallon of product). The proposed use is for handheld broadcast and soil-directed applications at a single maximum application rate of 0.0125 lb ai/gallon of solution and broadcast applications via ground and chemigation equipment at a single maximum application of 0.25 lb ai/acre. The proposed label allows a maximum of 2 applications per season with a re-treatment interval (RTI) of 14 days. Applicators and handlers are required to wear baseline attire (i.e., long-sleeve shirt, long pants and shoes plus socks) along with personal protective equipment (PPE) consisting of chemical-resistant gloves. Workers may not re-enter a treated area until 12 hours after application (restricted entry interval (REI) of 12 hours).

Exposure Profile

Based on the proposed use of ethaboxam, short- (1 to 30 days) and intermediate-term (1 to 6 months) occupational handler dermal and inhalation exposure is expected to occur. Additionally, short-term occupational dermal post-application activities are anticipated. Residential and non-occupational (resulting from spray drift) exposures are not expected from the proposed use as it is limited to greenhouses.

Hazard Characterization

The ethaboxam toxicology database is complete. The Hazard Science and Policy Council (HASPOC) recommended to waive the subchronic inhalation toxicity study (TXR 0056543, K. Rury, 03/20/2013). The toxicological doses and endpoints used for risk assessment have not changed since the most recent ethaboxam human health risk assessment (D464820, K. Chan, 09/08/2022).

Toxicological studies are available in rats, mice, rabbits, and dogs. In rats, alterations to the male reproductive organs, as well as functional effects on reproduction were seen in oral studies; however, no treatment-related effects on male reproductive organs were observed in studies with mice, rabbits, or dogs. Effects were seen in mouse liver and in dog thymus and spleen. No evidence of immunotoxicity was observed, and there is no concern for neurotoxicity. No evidence of increased quantitative or qualitative susceptibility was seen in the developmental toxicity studies in rats and

rabbits; however, increased qualitative susceptibility was seen in the rat reproduction study where decreased body weight, decreased viability, and delayed sexual maturation was seen in offspring in the presence of limited parental effects. HED based the risk assessment for ethaboxam on the most sensitive species and effects observed in the toxicological database; thus, points of departure (PODs) selected for risk assessment are protective of all treatment-related effects observed after exposure to ethaboxam. The 28-day dermal study in the rat was selected for short- and intermediate-term dermal exposure. The 13-week oral toxicity study in the rat was selected for the short- and intermediate-term inhalation endpoint. Dermal and inhalation exposures should not be combined since the toxicological effects for each route were not the same.

Ethaboxam is classified as having "Suggestive Evidence of Carcinogenicity," based on an increased incidence of benign Leydig cell tumors in male rats. The Agency has determined that quantification of cancer risk using a non-linear approach will adequately account for all chronic toxicity, including carcinogenicity, resulting from ethaboxam exposures (TXR 0054172, J. Kidwell, 03/23/2006).

Based on both hazard and exposure considerations, HED reduced the required 10X Food Quality Protection Act (FQPA) Safety Factor (SF) to 1X. The level of concern (LOC) for dermal and inhalation risk assessments is a margin of exposure (MOE) of 100, based on the combined interspecies (10X) and intraspecies (10X) uncertainty factors (UFs).

Residential Exposure and Risk

Residential exposure is not expected from the proposed greenhouse applications and there are no registered residential uses of ethaboxam; therefore, residential handler and post-application exposure was not quantitatively assessed.

Occupational Exposure and Risk

Short- and intermediate-term occupational handler dermal and inhalation risk estimates are not of concern (i.e., MOEs ≥ LOC of 100) for all scenarios when assessed 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. The risk estimates range from MOEs of 1,800 to 21,000 and 1,300 to 630,000 for dermal and inhalation exposure, respectively.

Short-term dermal occupational post-application exposures were not of concern with dermal MOEs ranging from 3,600 to 19,000 (LOC = 100) on the day of application (0-days after treatment (0-DAT)) for all post-application occupational activities using default dislodgeable foliar residue (DFR) assumptions.

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for ethaboxam 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 ethaboxam.

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 the ARTF database 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

There are no occupational handler dermal or inhalation risk estimates of concern (i.e., all MOEs ≥ the LOC of 100) for the proposed uses of ethaboxam, using baseline attire and no PPE. Risk estimates range from MOEs of 1,800 to 21,000 and 1,300 to 630,000 for dermal and inhalation exposure, respectively.

There are no occupational post-application dermal risk estimates of concern with dermal MOEs ranging from 3,600 to 19,000 (LOC = 100) for the proposed uses of ethaboxam on 0-DAT.

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. Dislodgeable foliar residue (DFR) data are recommended to be waived as specified below.

Since the highest estimated occupational post-application exposure using default DFR values for ethaboxam is minimal in comparison to the LOC (i.e., the calculated MOE is greater than 2 times higher than the LOC, MOE = 3,600 compared to the LOC of 100); HED is recommending waiving the 40CFR DFR data requirement. In this instance, it is unlikely that chemical-specific DFR data would be needed to further refine exposure assessments or would add appreciably to our overall understanding of the availability of dislodgeable foliar pesticide residues for ethaboxam.

3.0 Hazard Characterization

The toxicology database is complete for ethaboxam. HASPOC recommended to waive the subchronic inhalation toxicity study (TXR 0056543, K. Rury, 03/20/2013). The toxicological doses and endpoints

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

used for risk assessment have not changed since the most recent human health risk assessment, (D464820, K. Chan, 09/08/2022).

Acute Toxicity

Acute exposure to ethaboxam resulted in low toxicity and was classified as Category IV for all routes of exposure. Ethaboxam is not an eye irritant or dermal sensitizer. A summary of the acute toxicity profile is provided in Table 3.1 below.

Table 3.1. Acute Toxicity Profile for Ethaboxam (99.0%) Technical.

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute Oral (rat)	46378518	LD_{50} > 5000 mg/kg (M & F)	IV
870.1200	Acute Dermal (rat)	48535632	LD_{50} > 5000 mg/kg (M & F)	IV
870.1300	Acute Inhalation (rat)	48535633	LC_{50} > 4.89 mg/L (M & F)	IV
870.2400	Primary Eye Irritation (rabbit)	48535634	No corneal involvement or iritis observed. No positive conjunctival irritation in 1/3 rabbits at 24 hrs. (a score of 1 for redness) All irritation cleared by 48 hours.	IV
870.2500	Primary Skin Irritation (rabbit)	48535635	Not a dermal irritant	IV
870.2600	Dermal Sensitization (guinea pig)	48535636	Not a skin sensitizer (GPMT)	N/A

LD_{50} = median lethal dose, LC_{50} = median lethal concentration

Toxicological Points of Departure (PODs) Used for Risk Assessment

The 28-day dermal study in the rat was selected for short- and intermediate-term dermal exposure. The no-observed-adverse-effect level (NOAEL) of 300 mg/kg/day was based on decreased body weight and body weight gains at the lowest-observed-adverse-effect level (LOAEL) of 1,000 mg/kg/day. A route-specific inhalation toxicity study is not available for ethaboxam. In the absence of this study, the 13-week oral toxicity study in the rat was selected for the short- and intermediate-term inhalation endpoint. A NOAEL of 16.3 mg/kg/day was based on male reproductive effects and lung effects observed at the LOAEL of 650 ppm (49.7 and 58.0 mg/kg/day for males and females respectively). An UF of 100X (10X for extrapolation from animal to human and 10X for potential variation in sensitivity among members of the human population) is applied to the dermal and inhalation exposure scenarios.

Since the toxicological effects for the selected dermal and inhalation PODs are not the same, exposures from the different routes cannot be combined for risk assessment. A summary of the toxicological endpoints for ethaboxam is provided in Table 3.2 below.

Cancer Classification

In accordance with EPA's Final Guidelines for Carcinogen Risk Assessment (March, 2005), the Cancer Assessment Review Committee (CARC) classified ethaboxam as having "Suggestive Evidence of Carcinogenicity." Although there is evidence of benign Leydig cell tumors, the NOAEL used (5.5 mg/kg/day) for establishing the chronic reference dose is approximately 6-fold lower than the lowest dose that induced tumors (35.8 mg/kg/day). The Agency has determined that quantification of cancer risk using a non-linear approach would adequately account for all chronic toxicity (including any potential carcinogenicity) that could result from exposure to ethaboxam; therefore, a cancer assessment was not conducted (TXR 0054172, J. Kidwell, 03/23/2006).

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

Exposure/ Scenario	Point of Departure	Uncertainty / Safety Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Short-Term (1-30 days); Intermediate-Term (1-6 months)	NOAEL = 300 mg/kg/day	UF_A = 10X UF_H = 10X	Occupational LOC for MOE = 100	28-Day Dermal Toxicity – Rat (MRID 48535645) LOAEL (mg/kg/day): 1,000 mg/kg/day, based on decreased body weight and body weight gains.
Inhalation Short-Term (1-30 days); Intermediate-Term (1-6 months)	NOAEL = 16.3 mg/kg/day (Inhalation toxicity assumed to be equivalent to oral toxicity.)	UF_A = 10X UF_H = 10X	Occupational LOC for MOE = 100	13-Week Oral Toxicity – Rat (MRID 48535644) LOAEL (mg/kg/day): 49.7/58.0 mg/kg/day [M/F], based on testicular/epididymal effects in males (abnormal spermatids in the testes, and abnormal spermatogenic cells in the epididymides) and lung effects (increased lung weights, congestion, and alveolar septal congestion and focal alveolar hemorrhage).
Cancer (oral, dermal, inhalation)	Classification: "Suggestive Evidence of Carcinogenicity", based on increased incidence of Leydig cell tumors in males (TXR 0054172; J. Kidwell; 03/23/2006).			

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). LOC = level of concern. MOE = margin of exposure.

Absorption: Since the short- and intermediate-term dermal POD was based on a route-specific toxicity study, a dermal absorption factor (DAF) was not necessary to estimate exposure. Since inhalation absorption data are not available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure.

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 female-specific, developmental, and/or fetal effects.

4.0 Use Profile

V-10208 4 SC Fungicide is formulated as a suspension concentrate containing 42.5% ethaboxam (4 lb ai per gallon of product). The proposed use is for handheld broadcast and soil-directed applications at a single maximum application rate of 0.0125 lb ai/gallon of solution and broadcast applications via ground and chemigation equipment at a single maximum application of 0.25 lb ai/acre. The proposed label allows a maximum of 2 applications per season with a RTI of 14 days. Applicators and handlers are required to wear baseline attire (i.e., long-sleeve shirt, long pants and shoes plus socks) along with PPE consisting of chemical-resistant gloves. Workers may not re-enter a treated area until 12 hours after application (REI of 12 hours).

Table 4.1. Summary of Directions for Proposed Use of Ethaboxam on Leaf Petiole Vegetable (crop subgroup 22b) in Greenhouses.

Applic. Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Year	Max. Annual Applic. Rate	Use Directions and Limitations
Broadcast, Chemigation	Soluble Concentrate [59639-211]	0.25 lb ai/A	2	0.5 lb ai/A	RTI = 14 days. REI = 12 hours. PHI = N/A. PPE = chemical- resistant gloves made of any waterproof material, socks and shoes.
Broadcast, Groundboom					
Broadcast, Backpack		0.0125 lb ai/ gal solution*		0.025 lb ai/gal	
Broadcast, Manually-pressurized Handwand					
Broadcast, Mechanically-pressurized Handgun					
Drench/Soil-/Ground-directed, Mechanically-pressurized Handgun					

* Based on 20 gal/A application volume (i.e., [(0.25 lb ai/A ÷ 20 gal/A = 0.0125 lb ai/gal solution]).

5.0 Residential Exposure and Risk Estimates

There are currently no registered or proposed residential uses of ethaboxam; therefore, a quantitative residential exposure and risk assessment was not conducted. Additionally, there is no residential component available for inclusion in aggregate assessment of ethaboxam.

6.0 Non-Occupational Spray Drift Exposure and Risk Estimates

The proposed ethaboxam use is for applications in greenhouses. These uses are not likely to result in spray drift.

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

The proposed ethaboxam use is for applications in greenhouses. These uses are not likely to result in post-application inhalation exposure to individuals nearby greenhouse pesticide applications.

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, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed use in greenhouses.

The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios presented in Table 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: The ethaboxam quantitative exposure/risk assessment developed for occupational handlers is based on the proposed application rates listed 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 the AHETF database, ARTF 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[2]", 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[3].

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 ethaboxam, based on the proposed use, short- and intermediate-term exposures are expected.

Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated considering the PPE listed on product labels, and any additional PPE necessary to identify risk estimates not of concern. The attire and/or PPE that was considered and assessed include: baseline, defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator. The proposed ethaboxam product labels direct mixers, loaders, applicators

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

and other handlers to wear long-sleeved shirt and long pants, shoes plus socks, and chemical-resistant 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 exposure estimates were not combined since they were not based on the same toxicological effects.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates
MOEs with baseline attire (i.e., no gloves) ranged from 1,800 to 21,000 and 1,300 to 630,000 for dermal and inhalation exposure, respectively.

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 8.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Ethaboxam.

Exposure Scenario	Crop or Target	Dermal Unit Exposure (µg/lb ai)[1]	Level of PPE	Inhalation Unit Exposure (µg/lb ai)[1]	Level of PPE	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Dermal		Inhalation	
								Dose (mg/kg/day)[4]	MOE[5] (LOC = 100)	Dose (mg/kg/day)[6]	MOE[7] (LOC = 100)
Mixer/Loader											
Liquid, Chemigation, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	220	SL/No G	0.219	No-R	0.25 lb ai/acre	60 acres	0.0413	7,300	0.0000411	400,000
Liquid, Groundboom, Broadcast											
Applicator											
Spray (all starting formulations), Groundboom, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	78.6	SL/No G	0.34	No-R	0.25 lb ai/acre	60 acres	0.0148	20,000	0.0000638	260,000
Mixer/Loader/Applicator											
Liquid, Backpack, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	13,200	SL/No G	140	No-R	0.0125 lb ai/gallon solution	7 gallons solution	0.0145	21,000	0.000154	110,000
Liquid, Manually-pressurized Handwand, Broadcast		100,000		23.6				0.109	2,800	0.0000259	630,000
Liquid, Mechanically-pressurized Handgun, Broadcast		5,950		448			175 gallons solution	0.163	1,800	0.0123	1,300
Liquid, Mechanically-pressurized Handgun, Drench/Soil-/Ground-directed											

1. 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:

SL/No G = single layer, no gloves; No-R = no respirator).
2. Based on registered or proposed label (EPA Reg. No. 59639-211). See Table 4.1.
3. Exposure Science Advisory Council Policy #9.2.
4. Dermal Dose: 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 Daily (A or gal/day) ÷ BW (80 kg).
5. Dermal MOE: Dermal MOE = Dermal POD (300 mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100.
6. 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).
7. Inhalation MOE = Inhalation MOE = Inhalation POD (16.3 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). Level of concern (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 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 ethaboxam.

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.

The WPS for Agricultural Pesticides contains requirements for protecting workers from inhalation exposures during and after greenhouse applications through the use of ventilation requirements [40 CFR 170.110, (3) (Restrictions associated with pesticide applications)].

8.2.2 Occupational Post-application Dermal Exposure/Risk Estimates

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

[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

Transfer Coefficients: It is the policy of HED to use the best available data to assess post-application exposure. Sources of generic post-application data, used as surrogate data in the absence of chemical-specific data, are derived from ARTF exposure monitoring studies, and, as proprietary data, are subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting post-application exposure that are used in this assessment, known as "transfer coefficients", are presented in the ExpoSAC Policy 3[6] which, along with additional information about the ARTF data, can be found at the Agency website[7].

Application Rate: The ethaboxam quantitative exposure/risk assessment developed for occupational post-application workers is based on the proposed application rates listed in Table 4.1.

Exposure Time: The average occupational workday is assumed to be 8 hours.

DFR: Chemical-specific dislodgeable foliar residue data have not been submitted for ethaboxam. Therefore, this assessment uses HED's default assumption that 25% of the application is available for transfer on day 0 following the application and the residues dissipate at a rate of 10% each following day.

Occupational Post-application Non-Cancer Dermal Exposure and Risk Estimate Equations

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

Occupational Post-application Non-Cancer Dermal Risk Estimates

There are no occupational post-application risks of concern on the day of application on 0-DAT using default residue assumptions (i.e., all MOEs on day 0 ≥ the LOC).

Table 8.2.2.1 Occupational Post-application Non-Cancer Exposure and Risk Estimates for Ethaboxam on 0-DAT.

Crop/Site	Activities	Transfer Coefficient (cm^2/hr)	Application Rate (lb ai/A)	DFR[1]	Dermal Dose (mg/kg/day)[2]	MOE (LOC = 100)[3]
Greenhouse vegetable	Harvesting, Hand Pinching Pruning, Hand Scouting Weeding, Hand	1,200	0.25	0.70	0.084	3,600
	Transplanting	230			0.016	19,000

1. DFR = Application Rate (0.25 lb ai/A) × F × $(1\text{-}D)^t$ × 4.54E8 µg/lb × 2.47E-8 acre/cm^2; where F = 0.25 and D = 0.10 per day.
2. Daily Dermal Dose (mg/kg/day) = [DFR (µg/cm^2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day] ¸ BW (80 kg).
3. MOE = POD (300 mg/kg/day) / Daily Dermal Dose (mg/kg/day). Level of concern (LOC) = 100

Restricted Entry Interval

Ethaboxam is classified as Toxicity Category IV via the dermal route and Toxicity Category IV for skin and eye irritation potential. It is not a skin sensitizer. Short- and intermediate-term post-application risk estimates were not a concern on day 0 immediately following application for all post-application

[6] Available online: Science Advisory Council for Exposure (ExpoSAC) (epa.gov)

[7] Available online: Occupational Pesticide Post-application Exposure Data | US EPA

activities. Under 40 CFR 156.208 (c) (2), ai's 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] WPS interim REI of 12 hours is adequate to protect agricultural workers from post-application exposures to ethaboxam. HED would recommend a REI of 12 hours. This is the REI listed on the proposed label and is considered protective of post-application exposure.

Appendix A. Summary of Occupational 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).

Occupational Non-cancer Post-application Algorithms

Potential daily exposures for occupational post-application workers are calculated using the following formulas:

$$DFR_t = AR * F * (1-D)^t * \left(4.54E8 \frac{ug}{lb}\right) * \left(2.47E\text{-}8 \frac{A}{cm^2}\right)$$

where:

DFR_t	=	dislodgeable foliage residue on day "t" (µg/cm^2),
AR	=	application rate (lb ai/acre),
F	=	fraction of ai retained on foliage or 25% (unitless),
D	=	fraction of residue that dissipates daily or 10% (unitless), and
t	=	number of days after application day (days).

$$E = TC * DFR_t * ET * 0.001 \frac{mg}{ug}$$

where:

E	=	exposure (mg ai/day),
TC	=	transfer coefficient (cm^2/hr),
DFR_t	=	dislodgeable foliar residue on day “t” (µg/cm^2), and
ET	=	exposure time (hours/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 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 dose received by occupational post-application workers is compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational post-application workers. 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).