OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

MEMORANDUM

DATE: May 8th, 2024

SUBJECT: **Indoxacarb**. Human Health Risk Assessment for Section 3 Registration in/on Coffee, Strawberry, and Sunflower Crop Subgroup 20B; and Crop Group Conversions and Expansions.

PC Code: 067710
CAS No.: 173584-44-6
Decision No.: 591203
Petition No.: 2E9044
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D467782
Task Group No.: 00484551
Parent Case No.: 00472648
Registration No.: 279-9629, 279-9596
Regulatory Action: Section 3
Reg Review Case No.: 7613
40 CFR: §180.564

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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, as needed, in support of a Section 3 registration for the proposed new uses and crop group expansions/conversions of indoxacarb. Indoxacarb is an oxadiazine insecticide currently registered on a variety of agricultural and non-agricultural use sites.

Interregional Research Project No. 4 (IR-4) is requesting the following actions for indoxacarb:

- Proposed new food uses in/on coffee, strawberry, and sunflower subgroup 20B. Residue field trial data have been submitted in support of this request.

- Crop group expansions for existing registrations to cottonseed subgroup 20C; edible podded bean subgroup 6-22A and succulent shelled bean subgroup 6-22C (from bean, succulent); pulses, dried shelled bean, except soybean, subgroup 6-22E (from bean, dried); field corn subgroup 15-22C; and sweet corn subgroup 15-22D.

- Crop group conversions to update existing registrations to include leafy greens subgroup 4-16A; brassica, leafy greens subgroup 4-16B; vegetable, Brassica, head and stem group 5-16; and vegetable fruiting, group 8-10; fruit, pome, group 11-10, except pear; fruit, stone, group 12-12; pear, Asian, and leaf petiole vegetable subgroup 22B.

HED notes that the International Organization for Standardization (ISO) defines indoxacarb to be the insecticidally active S-enantiomer. Indoxacarb products are produced as the insecticidally active S-enantiomer or a mixture of the S-enantiomer and the insecticidally inactive R-enantiomer. The percent active ingredient (ai) and application rates listed on indoxacarb product labels reflect only the S-enantiomer; labels do not reflect the amount of R-enantiomer in the mixtures. Toxicological equivalency has been established for the formulated indoxacarb products. In this risk assessment, the term indoxacarb refers to the S-enantiomer; however, this risk assessment considers both enantiomers because the analytical method does not distinguish between them.

This memorandum serves as the Agency's assessment of the human health risks from the proposed uses and crop group expansions/conversions of indoxacarb.

Table of Contents

1.0 Executive Summary

RD has requested that HED conduct an exposure and risk assessment, as needed, in support of Section 3 Registration for the proposed new uses and crop group expansions/conversions of indoxacarb. There are no residential uses and/or non-agricultural use sites being proposed as part of this registration. This memorandum serves as the Agency's assessment of the human health risks from the proposed uses and crop group expansions/conversions of indoxacarb.

Use Profile: IR-4 has submitted two proposed end-use product labels for the requested new uses of indoxacarb.[1] For sunflower, Steward EC [EPA Reg. No.: 279-9596] is formulated as an emulsifiable concentrate (EC) containing 15.84% of the ai indoxacarb with a single use maximum application rate of 0.11 lb ai/A. For coffee and strawberry, Avuant Evo [EPA Reg. No.: 279-9629] is formulated as a soluble granular (SG) containing 30.0% of the ai indoxacarb with a single use maximum application rate of 0.11 lb ai/A. Both end-use products are intended for foliar applications via aerial, ground (airblast, groundboom, or mechanically-pressurized handguns), or chemigation, where specified. The pre-harvest intervals (PHIs) range from 1-28 days (specified based on crop type). The proposed labels require that all applicators/handlers wear baseline attire (*i.e.,* single layer of clothes defined as long-sleeved shirt, long pants, shoes, and socks) and the following personal protective equipment (PPE): chemical-resistant gloves and respirator (where applicable).[2] A restricted entry interval (REI) of 12 hours is listed on the proposed labels.

HED notes that in addition to the details provided above, the proposed labels include the requested crop group expansions/conversions revisions, where specified. These revisions do not impact the use profiles of any current registrations. In support of this request, the use profiles for the requested crop group expansions/conversions are summarized in Table 3.3 of this memo. A detailed review of the assessed use patterns, application rates, and restrictions for these uses are provided in D444002 (U. Hassan, 24-OCT-2017) and D438791 (U. Hassan, 22-JUN-2017).

Exposure Profile: Humans may be exposed to indoxacarb in food and drinking water since indoxacarb may be applied directly to growing crops and following harvest, and application may result in indoxacarb reaching surface and ground sources of drinking water. In an occupational setting, applicators may be exposed while handling the pesticide prior to application as well as during application. There is also potential for post-application exposure for workers re-entering treated fields. There are no new residential uses proposed for indoxacarb; however, there are currently-registered residential uses that would result in residential handler exposures for adults and post-application exposures for adults and children. Non-occupational exposure resulting from spray drift from agricultural applications onto residential areas may also occur.

[1] Indoxacarb products may consist of a mixture of the insecticidally active S-enantiomer and the insecticidally inactive R-enantiomer, or S-enantiomer only formulations. The percent active ingredient and application rates listed on indoxacarb product labels only reflect the insecticidally active S-enantiomer; labels do not reflect the amount of any inactive R-enantiomer in the mixture.

[2] End-use product Avaunt Evo requires that mixers and loaders supporting aerial applications to dried and/or succulent beans must wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters.

Hazard Characterization: The toxicological database for indoxacarb is complete. Previously submitted studies used to determine toxicological endpoints and points of departure (PODs) for indoxacarb, in addition to a full characterization of the hazard, is provided in D453637 (H. DeLeon, 20-AUG-2020). No new toxicological studies/data have been submitted in support of this action; therefore, the toxicological endpoints and PODs remain current and are summarized in Section 4.1 of this assessment.

Residue Chemistry: The proposed uses and tolerances are supported by sufficient crop field trial data and processing studies. Storage intervals and conditions for the samples collected in the field trials and processing studies are acceptable based on storage stability data generated concurrently with the studies. Samples were analyzed using validated methods, and acceptable processing studies were conducted for the appropriate processed commodities. The proposed tolerances are not expected to raise the livestock dietary burden; therefore, the currently established livestock tolerances for indoxacarb remain appropriate.

Dietary Exposure Assessment: A partially-refined acute probabilistic dietary (food and drinking water) exposure assessment was conducted for indoxacarb. The acute dietary risk estimates are not of concern (i.e., < 100% of the acute population adjusted dose (aPAD)) at the 99.9th percentile. Children (1-2 years old) is the most highly exposed population subgroup, occupying 57% of the aPAD at the 99.9th percentile; while the general US population acute exposure occupies 33% of the aPAD at the 99.9th percentile. A partially-refined chronic dietary (food and drinking water) exposure assessment was conducted for indoxacarb as well. The chronic dietary risk estimates are not of concern (i.e., < 100% of the chronic population adjusted dose (cPAD)). All infants (< 1 year old) is the most highly exposed population subgroup, occupying 50% of the cPAD; while the general US population chronic exposure occupies 15% of the cPAD.

Residential Exposure and Risk Assessment: Residential (handler and post-application) exposures are not anticipated from the proposed new uses of indoxacarb. Therefore, quantitative residential handler and post-application risk assessments were not conducted in support of this action. However, there are currently registered uses of indoxacarb that may result in residential handler and post-application exposures. Those residential uses have been assessed previously in D453658 (H. DeLeon, 26-AUG-2019) and are not of concern. HED's residential risk estimate recommendations for use in aggregate human health risk assessment remain current and are summarized in Section 6.0.

Aggregate Risk Assessments: There are no aggregate risk estimates of concern resulting from the proposed new uses and/or crop group expansions/conversions of indoxacarb. For indoxacarb, the acute aggregate risks are equivalent to the acute dietary risks and were not of concern (See Section 5.4.3). Since there is no dermal hazard identified for indoxacarb and inhalation exposures cannot be aggregated with oral exposures due to differences in the toxicological endpoints/PODs, a short-term aggregate assessment is not conducted for adults; and the chronic aggregate risk for adults is equivalent to the chronic dietary risk and is not of concern (See Section 5.4.4).

For children (1 to<2 years old), there are short-/intermediate- and long-term residential exposures (incidental oral exposures from pet uses) that can be aggregated with dietary exposure. For children, the short-/intermediate-/long-term aggregate MOEs range from 120 to 250; which are above the level of concern (LOC) of 100 and are not of concern.

Occupational Exposure and Risk Assessment: Since no dermal hazard was identified for indoxacarb, quantitative occupational handler/post-application assessments for dermal exposures were not conducted at this time. Occupational handler inhalation exposures were assessed for the proposed new uses of indoxacarb only. For the proposed new uses of indoxacarb, the inhalation MOEs range from 65 to 120,000 for occupational handlers wearing label-specified baseline attire/PPE (i.e., single layer clothing and no respirator), which are above the LOC of 30 and not of concern.

Occupational handler exposure and risk assessments for crops included in the crop group expansions/conversions were not conducted at this time as representative crop scenarios were assessed previously in D444002 (U. Hassan, 24-OCT-2017) and D438791 (U. Hassan, 22-JUN-2017). Since the use patterns, application rates, and equipment for these exposure scenarios remain unchanged, the previously-calculated occupational risk estimates for these scenarios remain current and are protective of the requested crop group expansions/conversions.[3] There are no occupational handler inhalation risks of concern (*i.e.,* MOEs ≥ the LOC of 30) identified for the requested crop group expansions/conversions of indoxacarb.

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

Environmental Justice: Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations.[4]"

Human Studies: This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide to determine their exposure. Appendix C provides additional information on the review of human research used to complete the risk assessment. There is no regulatory barrier to continued reliance on these studies, and all applicable requirements of EPA's Rule for the Protection of Human Subjects of Research (40 CFR Part 26) have been satisfied see Appendix C).

2.0 HED Recommendations

2.1 Data Deficiencies

Pending submission of a revised Section F (see requirements under Revisions to Petitioned-For Tolerances, section 2.2.2 below), there are no data deficiencies that would preclude establishing the recommended tolerances for the proposed new uses of indoxacarb.

[3] See D444002 (U. Hassan, 24-OCT-2017) and D438791 (U. Hassan, 22-JUN-2017) for a detailed review of assessed occupational handler exposure scenarios, assessment parameters, and calculated risk estimates.

[4] https://www.epa.gov/laws-regulations/summary-executive-order-12898-federal-actions-address-environmental-justice

Analytical standards for indoxacarb (racemic and S-enantiomer) and metabolite JT333 are available at the EPA National Pesticide Repository, as indicated in the table below (electronic communication with Craig Vigo on 15-SEP-2023). The registrant must replenish supplies of these standards prior to expiration.

Chemical	Expiration Date
Indoxacarb (racemic); CAS #:144171-61-9	11-APR-2028
Indoxacarb (S-enantiomer); CAS #:173584-44-6	05-DEC-2024
Indoxacarb, metabolite of S- enantiomer, JT333; CAS #: NA	03-AUG-2026

However, 1-gram standards for each of the regulated metabolites of indoxacarb, shown in the table below, should be submitted to the National Pesticide Standards Repository. The address to submit standards is below and should be submitted to the attention of Craig Vigo; the full 9-digit zip code is mandatory, or the mail will be returned to the sender.

U.S. EPA National Pesticide Standard Repository; Attn: Craig Vigo
Environmental Science Center
701 Mapes Road, Suite 5350
Fort Meade, MD 20755-5350

Compound	CAS Name	CAS #
IN-JU873	Methyl 5-chloro-2,3-dihydro-2-hydroxy-1-[[[[4-(trifluoromethoxy)phenyl]amino]-carbonyl]hydrazono]-1H-indene-2-carboxylate	144172-25-8
IN-KB687	Methyl [4-(trifluoromethoxy)phenyl]-carbamate	177905-10-1
IN-KT319	(*E*)-methyl 5-chloro-2,3-dihydro-2-hydroxy-1-[[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]-carbonyl]hydrazono]-l*H*-indene-2-carboxylate	None
IN-KG433	(*Z*)-Methyl 5-chloro-2,3-dihydro-2-hydroxy-1-[[[(methoxycarbonyl)[4-trifluoromethoxy) phenyl]amino]carbonyl]hydrazono]-1*H*-indene-2-carboxylate	None

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

Adequate analytical methods are available for enforcing indoxacarb tolerances on both plant and livestock commodities. Because these methods do not distinguish the indoxacarb enantiomers, they give a total measure of indoxacarb concentration.

Crops: For the enforcement of tolerances established on crops, two High Performance Liquid Chromatograph/Ultraviolet Detection (HPLC/UV) methods, DuPont protocols AMR 2712-93 and DuPont-11978, are available for use. The limits of quantitation (LOQs) for these methods range from 0.01 to 0.05 ppm for a variety of plant commodities. A third Gas Chromatograph/Mass-Selective Detection (GC/MSD) procedure, DuPont method AMR 3493-95 Supplement No. 4, is also available for the confirmation of residues in plants. In addition, a Liquid Chromatograph/Mass Spectrometer/Mass Spectrometer (LC/MS/MS) method, Method Dupont-36189, has been developed and is considered an improvement of the previously-approved enforcement method, Method DuPont-AMR-2712-93. Method DuPont-36189 has been determined to be adequate for enforcing tolerances established on crops and is reported to provide an LOQ of 0.01 ppm.

Livestock: For the enforcement of livestock tolerances, an HPLC/column switching/UV Method (AMR 3337-95) can determine the parent compound as well as the metabolite IN-JT333. This method has been demonstrated to provide an LOQ of 0.01 ppm with a reported limit of detection (LOD) of 0.002-0.003 ppm. For poultry commodity analyses, an LC/MS/MS method, AMR 12739, was developed by DuPont; this method has been successfully validated using hen muscle, liver, skin, and fat as well as, whole egg, egg yolk, and egg white samples.

2.2.2 Recommended Tolerances

The current tolerance expression for indoxacarb established in 40 CFR §180.564(a) is adequate. Table 2.2.2 summarizes the tolerances recommended in for the proposed new food uses and the requested crop group expansions/conversions for indoxacarb (D468389, E. Ford, 08-MAY-2023). These tolerances will be added to the table located at 40 CFR § 180.564(a)(1).

Table 2.2.2. Tolerance Summary for Indoxacarb.

Commodity[1]	Established Tolerance (ppm)	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
***Brassica*, leafy greens, subgroup 4-16B**	--	12	12	Conversion from vegetable, *Brassica*, leafy, group 5 at 12 ppm
Turnip, greens	12	Remove	Remove	
Vegetable, Brassica, leafy, group 5	12	Remove	Remove	
Celtuce	--	14	14	Included in group 4 but not 4-16A; follows use directions for celery
Chickpea, dry seed	--	0.2	0.2	Based on bean, dry
Coffee, green bean	--	0.03	0.03	
Cottonseed subgroup 20C	--	2	2	Expansion from cotton, undelinted seed at 2.0 ppm
Cotton, undelinted seed	2.0	Remove	Remove	
Fennel, florence, fresh leaves and stalk	--	14	14	Included in group 4 but not 4-16A; follows use directions for celery
Field corn subgroup 15-22C	--	0.02	0.02	Expansion from corn, field, grain at 0.02 ppm
Corn, field, grain	0.02	Remove	Remove	
Corn, pop, grain	0.02	Remove	Remove	
Fruit, pome, group 11-10, except pear	--	1	1	Conversion from fruit, pome, except pear, group 11 at 1.0 ppm
Fruit, pome, except pear, group 11	1.0	Remove	Remove	
Fruit, stone, group 12-12	--	1	1	Conversion from fruit, stone, group 12 at 0.90 ppm; harmonization with Codex
Fruit, stone, group 12	0.90	Remove	Remove	
Kohlrabi	--	12	12	Included in group 5 but not 4-16B (now 22A); follows use directions for cabbage and broccoli
Leaf petiole vegetable subgroup 22B	--	14	14	Conversion from vegetable, leafy, except *Brassica*, group 4 at 14 ppm
Leafy greens subgroup 4-16A	--	14	14	
Vegetable, leafy, except Brassica, group 4	14	Remove	Remove	
Pear, asian	--	0.2	0.2	Conversion from pear, oriental at 0.2 ppm
Pear, oriental	0.20	Remove	Remove	
Strawberry	--	4	4	
Sunflower subgroup 20B	--	1.5	1.5	
Sweet corn subgroup 15-22D	--	0.02	0.02	Expansion from corn, sweet, kernel plus cob with husk removed at 0.02 ppm
Corn, sweet, kernel plus cob with husk removed	0.02	Remove	Remove	
Vegetable, *brassica*, head and stem, group 5-16	--	12	12	Conversion from vegetable, *Brassica*, leafy, group 5 at 12 ppm

Table 2.2.2. Tolerance Summary for Indoxacarb.				
Commodity[1]	**Established Tolerance (ppm)**	**Proposed Tolerance (ppm)**	**HED-Recommended Tolerance (ppm)**	**Comments**
Vegetable, legume, bean, edible podded, subgroup 6-22A	--	0.9	0.9	Expansion from bean, succulent at 0.9 ppm
Vegetable, legume, bean, succulent shelled, subgroup 6-22C	--	0.9	0.9	
Bean, succulent	0.9	Remove	Remove	
Pea, southern, seed	0.10	Remove	Remove	
Vegetable, legume, pulse, bean, dried shelled, except soybean, subgroup 6-22E	--	0.2	0.2	Expansion from bean, dry seed at 0.2 ppm
Bean, dry seed	0.2	Remove	Remove	
Vegetable, fruiting, group 8-10	--	0.5	0.5	Conversion from vegetable, fruiting, group 8 at 0.50 ppm
Okra	0.50	Remove	Remove	
Vegetable, fruiting, group 8	0.50	Remove	Remove	

[1] Correct commodity definition listed in **bold**.

2.2.3 Revisions to Petitioned-For Tolerances

HED does not recommend any revisions to the petitioned-for tolerances.

2.2.4 International Harmonization

An International Residue Limit status sheet, including the commodities for which tolerances are recommended, is provided in Attachment A. Canada does not have tolerances established for indoxacarb. However, Codex has MRLs established on a number of plant and livestock commodities. The US and Codex are harmonized with respect to the residue definition for the commodities included in this petition. The proposed tolerance levels are not harmonized with Codex commodity MRLs for the following groups/subgroups: cottonseed subgroup 20C; fruit, pome, group 11-10, except pear; leafy greens subgroup 4-16A; vegetable, brassica, head and stem, group 5-16; vegetable, legume, pulse, bean, dried shelled, except soybean, subgroup 6-22E (dry cowpea only) and vegetable, fruiting, group 8-10 (peppers only). Harmonization of these groups/subgroups is not possible because the US tolerance is higher than the corresponding MRLs established by Codex; harmonization of the US tolerance to the lower Codex MRLs would not be protective of potential residues based on the residue data submitted to the US.

For cases in which the US tolerance is lower than the corresponding MRL, HED recommends increasing the US tolerance to match the MRL of international authorities. As such, HED concurs with IR-4's request to set the fruit, stone, group 12-12 tolerance at 1 ppm to harmonize with Codex's stone fruit group tolerance.

2.3 Label Recommendations

2.3.1 Recommendations from Residue Reviews

There are no specific label recommendations. However, HED notes that the current crop group nomenclature on the provided labels is not consistent with the requested crop group

expansions/conversions specified in IR-4's request. HED requests that RD review the proposed labels to ensure the appropriate revisions/updates are made to adequately reflect the requested crop group expansions/conversions.

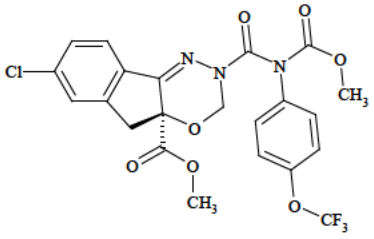
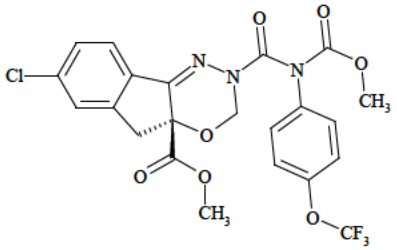
2.3.2 Recommendations from Occupational Exposure Assessment

None.

Note on mixing/loading liquid formulation scenarios: A 2019 study by the Agricultural Handler Exposure Task Force (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.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. Indoxacarb Nomenclature.	
Compound	
Common name	Indoxacarb S-enantiomer
Company experimental name	DPX-KN128 (pesticidally active)
IUPAC name	(S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3*H*)-carboxylate
CAS name	methyl (4aS)-7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylate
CAS registry number	173584-44-6
End-use product (EP) for the proposed use	30% WDG DuPont™ Avaunt® eVo (EPA Reg. No. 279-9629) formulated solely with the 98% ai (DPX-KN128; aka KN128) technical substance.
Compound	
Common name	Indoxacarb R-enantiomer
CAS registry number	185608-75-7
Company experimental name	IN-KN127 (pesticidally inactive)

3.2 Physical/Chemical Characteristics

Indoxacarb is an oxadiazine pesticide developed by DuPont that is formed as a white granule. Indoxacarb has a very low vapor pressure of 1.9 x 10^{-10} mm Hg at 25°C; volatilization is not expected to be a significant route of dissipation for this pesticide. The octanol water partition coefficient (Log K_{OW} = 4.65) suggests that it is lipophilic. Indoxacarb is slightly soluble in water (0.8 mg/L at pH 7 at 20°C). Indoxacarb is considered to be moderately persistent, with aerobic half-lives ranging from 3 to 693 days and anaerobic half-lives ranging from 147 to 233 days. It is considered immobile with K_{ocs} ranging from 3,300 to 9,600 ml/g. The physical and chemical properties of indoxacarb are detailed in Table B.1 of Appendix B.

3.3 Pesticide Use Pattern

Table 3.3 summarizes the use patterns for the proposed new food uses and crop group expansions/conversions.

Table 3.3. Summary of Proposed Use Patterns and Directions for Indoxacarb.

Application Equipment Formulation [EPA Reg. No.]	Crop Type/Group	Application Type	Single Use Max App Rates [1]	Use Directions and Limitations [2]
New Uses				
Aerial; Ground; Chemigation Soluble Granule (SG) 30.0% Indoxacarb [279-9629]	Coffee	Aerial and Ground Foliar Broadcast	0.11 lb ai/A	▪ PPE required and an REI of 12 hours. ▪ RTI of 7 days. ▪ PHI for coffee is 14 days; and 1 day for strawberry. ▪ Minimum of 5 GPA for aerial applications. ▪ Minimum of 10 GPA for ground applications. ▪ No more than 4 applications per year.
	Strawberry			
Aerial; Ground; Chemigation Emulsifiable Concentrate (EC) 15.84% Indoxacarb 1.25 lb ai/gal [279-9596]	Sunflower, Subgroup 20B	Aerial and Ground Foliar Broadcast	0.11 lb ai/A	▪ PPE required and an REI of 12 hours. ▪ RTI of 5 days. ▪ PHI of 14 days. ▪ Minimum of 3 GPA for aerial applications. ▪ Minimum of 5 GPA for ground applications. ▪ No more than 4 applications per year.
Crop Group Expansions				
Aerial; Ground; Chemigation Soluble Granule (SG) 30.0% Indoxacarb [279-9629]	Spinach	Aerial, Ground, and Chemigation Foliar Broadcast	0.065 lb ai/A	▪ PPE required and an REI of 12 hours. ▪ Minimum RTI's range from 3 to 7 days. ▪ PHI's range from 3 to 7 days. ▪ Minimum spray volumes for aerial applications range from 3 to 5 GPA. ▪ Minimum spray volumes for ground applications range from 10 to 20 GPA. ▪ No more than 4 applications per year.
	Sweet Corn, Subgroup 15-22D			
	Edible Podded Bean, Subgroup 6-22A	Aerial and Ground Foliar Broadcast	0.11 lb ai/A	
	Succulent Shelled Bean, Subgroup 6-22C			
	Pulses, Dried Shelled Bean, Subgroup 6-22E (Except Soybean)			

Table 3.3. Summary of Proposed Use Patterns and Directions for Indoxacarb.

Application Equipment Formulation [EPA Reg. No.]	Crop Type/Group	Application Type	Single Use Max App Rates [1]	Use Directions and Limitations [2]
Aerial; Ground; Chemigation Emulsifiable Concentrate (EC) 15.84% Indoxacarb 1.25 lb ai/gal [279-9596]	Cottonseed Subgroup 20C	Aerial, Ground, and Chemigation Foliar Broadcast	0.11 lb ai/A [0.022 lb ai/gal][1]	▪ PPE required and an REI of 12 hours. ▪ Minimum RTI's range from 5 to 7 days. ▪ PHI for subgroup 20C is 14 days; 7 days for subgroup 6-22E; and 1-14 days for subgroup 15-22C. ▪ Minimum spray volumes for aerial applications range from 3 to 5 GPA. ▪ Minimum spray volumes for ground applications range from 5 to 20 GPA. ▪ No more than 4 application per year. ▪ For 15-22C, make no more than 2 applications per acre per crop.
	Field Corn Subgroup 15-22C			
	Pulses, Dried Shelled Bean, Subgroup 6-22E (Except Soybean)	Aerial and Ground Foliar Broadcast	0.11 lb ai/A	
Crop Group Conversions				
Aerial; Ground; Chemigation Soluble Granule (SG) 30.0% Indoxacarb [279-9629]	Leafy Greens, Subgroup 4-16A (Except Spinach)	Aerial and Ground Foliar Broadcast	0.11 lb ai/A	▪ PPE required and an REI of 12 hours. ▪ Minimum RTI is 3 days. ▪ PHI for these subgroups is 3 days. ▪ Minimum spray volumes for aerial applications are 5 GPA. ▪ Minimum spray volumes for ground applications are 10 GPA. ▪ No more than 4 applications per year.
	Brassica Leafy Greens, Subgroup 4-16B			
	Brassica Head and Stem Vegetables, Crop Group 5-16			
	Leaf Petiole Vegetables, Subgroup 22B			
	Fruiting Vegetables Crop Group 8-10	Aerial and Ground Foliar Broadcast	0.11 lb ai/A [0.011 lb ai/gal][1]	▪ PPE required and an REI of 12 hours. ▪ Minimum RTI's range from 5 to 7 days. ▪ PHI range from 3 days to 28 days. ▪ Minimum spray volumes for aerial applications range from 5 to 10 GPA. ▪ Minimum spray volumes for ground applications range from 10 to 50 GPA. ▪ No more than 4 applications per year. ▪ For CG 12-12: Make no more than 3 applications prior to hand-thinning. No hand-thinning after the 4th application.
	Chickpea, Dry Seed Subgroup 6-22B			
	Pome Fruit, Crop Group 11-10 (Except Pear)			
	Stone Fruit, Crop Group 12-12			
	Pear			

[1] Ground Applications: Minimum spray volume of 5 gallons per acre: [0.11 lb ai/A÷ 5 gallons spray volume/A] = 0.022 lb ai/gal. Minimum spray volume of 10 gallons per acre: [0.11 lb ai/A÷ 0 gallons spray volume/A] = 0.011 lb ai/gal

[2] PPE = personal protective equipment: the proposed label indicates that all applicators/handlers wear baseline attire (defined as: long-sleeved shirt, long pants, shoes, and socks); chemical resistant gloves; and respirator for mixers and loaders supporting aerial applications to dried and/or succulent beans. REI = restricted entry interval. RTI = re-treatment interval. PHI = pre-harvest interval. GPA = gallons per acre.

3.4 Anticipated Exposure Pathways

Humans may be exposed to indoxacarb in food and drinking water since indoxacarb may be applied directly to growing crops and following harvest, and application may result in indoxacarb reaching surface and ground sources of drinking water. In an occupational setting, applicators may be exposed while handling the pesticide prior to application as well as during application. There is also potential for

post-application exposure for workers re-entering treated fields. There are no new residential uses proposed for indoxacarb; however, there are currently registered residential uses that would result in residential handler exposures for adults and post-application exposures for adults and children. Non-occupational exposure resulting from spray drift from agricultural applications onto residential areas may also occur.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (https://www.archives.gov/files/federal-register/executive-orders/pdf/12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Spray drift can also potentially result in post-application exposure, and it is also being considered whenever appropriate. Further considerations are also currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to other types of possible bystander exposures and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

The toxicological database for indoxacarb is complete. A summary of previously-submitted studies used to determine toxicological endpoints and PODs for indoxacarb, as well as a full characterization of the hazard, is provided in D453637 (H. DeLeon, 20-AUG-2020). No new toxicological studies/data have been submitted in support of this action; therefore, the toxicological endpoints and PODs remain current and are summarized in Table 4.1.1 below.

4.1 Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Table 4.1.1. Points of Departure and Toxicological Endpoints Selected for Indoxacarb for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure Scenario	POD	UF, FQPA SF, and LOC	Study and Toxicological Effects
Acute Dietary all populations	NOAEL= 12 mg/kg	UF_A= 10X UF_H=10X FQPA SF = 1X **Acute RfD** = **aPAD** = 0.12 mg/kg	Acute oral rat neurotoxicity study. MRID 44477127 LOAEL = 50 mg/kg based on decreased body weight and body-weight gain in females (MP062).
Chronic Dietary all populations	NOAEL= 2.0 mg/kg/day	UF_A= 10X UF_H=10X FQPA SF = 1X **Chronic RfD** = **cPAD** = 0.02 mg/kg/day	Weight of evidence approach was used from four studies: 1) Subchronic toxicity study- rat (MP062). MRID 44477129. LOAEL = 6.0 (M), 3.8 (F) mg/kg/day based on decreased body weight, body-weight gain, food consumption and food efficiency. 2) Subchronic neurotoxicity study - rat (MP062). MRID 44477135. LOAEL = 5.6 (M), 3.3 (F) mg/kg/day based on decreased body weight and alopecia. 3) Chronic/carcinogenicity study - rat (JW062). MRID 44477145. LOAEL = 10 (M), 3.6 (F) mg/kg/day based on decreased body weight, body-weight gain, and food consumption and food efficiency; decreased HCT, HGB and RBC at 6 months in F only. 4) Two generation rat reproduction study (JW062). MRID 44477144 LOAEL = 4.4 mg/kg/day based on decreased body weights, body-weight gain, food consumption and food efficiency and increased spleen weights in the F_0 and F_1 females.
Short -Term Incidental Oral	NOAEL= 2.0 mg/kg/day	UF_A= 10X UF_H=10X FQPA SF = 1X LOC = 100	Weight of evidence approach was used from four studies: 1) Subchronic toxicity study- rat (MP062). MRID 44477129. LOAEL = 6.0 (M), 3.8 (F) mg/kg/day based on decreased body weight, body-weight gain, food consumption and food efficiency. 2) Subchronic neurotoxicity study - rat (MP062). MRID 44477135. LOAEL = 5.6 (M), 3.3 (F) mg/kg/day based on decreased body weight and alopecia. 3) Chronic/carcinogenicity study - rat (JW062). MRID 44477145. LOAEL = 10 (M), 3.6 (F) mg/kg/day based on decreased body weight, body-weight gain, and food consumption and food efficiency; decreased HCT, HGB and RBC at 6 months in F only. 4) Two generation rat reproduction study (JW062). MRID 44477144 LOAEL = 4.4 mg/kg/day based on decreased body weights, body-weight gain, food consumption and food efficiency, and increased spleen weights in the F_0 and F_1 females.
Short-Term Dermal (1 to 30 days) Intermediate-Term Dermal (1 - 6 months)	A quantitative dermal assessment is not required for indoxacarb since the calculated human dermal LOAEL exceeds the limit dose of 1000 mg/kg/day.		
Short-Term Inhalation (1 to 30 days) Intermediate-Term Inhalation (1 - 6 months)	NOAEL= 23 µg/L/day	UF_A= 3X UF_H=10X FQPA SF = 1X LOC = 30	28-day rat inhalation toxicity study (MP062). MRID 45870001 The LOAEL of 290 µg/L/day is based on increased spleen weights, pigmentation and hematopoiesis in the spleen, hematological changes, mortality (females), and nasal ulceration and inflammation. Note: The HEC used for the endpoint was based on the nasal effects. This HEC was lower than the systemic effects.

Table 4.1.1. Points of Departure and Toxicological Endpoints Selected for Indoxacarb for Use in Dietary and Non-Occupational Human Health Risk Assessments.			
Exposure Scenario	**POD**	**UF, FQPA SF, and LOC**	**Study and Toxicological Effects**
Cancer (oral, dermal, inhalation)	"Not likely" to be carcinogenic to humans since no evidence of carcinogenicity in either the rat or mouse studies, and no evidence of mutagenicity (TXR 0052478, P. Terse, 12-APR-2004).		

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). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. LOC = level of concern.

Table 4.1.2. Points of Departure and Toxicological Endpoints Selected for Indoxacarb for Use in Occupational Human Health Risk Assessments			
Exposure Scenario	**POD**	**UF and LOC**	**Study and Toxicological Effects**
Short-Term Dermal (1 to 30 days) Intermediate-Term Dermal (1 - 6 months)	A quantitative dermal assessment is not required for indoxacarb since the calculated human dermal LOAEL exceeds the limit dose of 1000 mg/kg/day.		
Short-Term Inhalation (1 to 30 days) Intermediate-Term Inhalation (1 - 6 months)	NOAEL = 23 µg/L/day	UF_A= 3X UF_H=10X LOC = 30	28-day rat inhalation toxicity study (MP062). The LOAEL of 290 µg/L/day is based on increased spleen weights, pigmentation and hematopoiesis in the spleen, hematological changes, mortality (females), and nasal ulceration and inflammation. Note: The HEC used for the endpoint was based on the nasal effects. This HEC was lower than the systemic effects.
Cancer (oral, dermal, inhalation)	"Not likely" to be carcinogenic to humans since no evidence of carcinogenicity in either the rat or mouse studies, and no evidence of mutagenicity (TXR 0052478, P. Terse, 12-APR-2004).		

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.

Table 4.1.3. Calculated Inhalation Human Equivalent Concentrations and Doses for Indoxacarb.[1]					
Population	**Scenario**	**Exposure Duration**	**HEC**		**HED**
		hours/day	**mg/L**	**mg/m**	**mg/kg/day**
Occupational	Handler	8	0.003	2.915	0.28
Residential	Handler	2	0.004	3.887	0.09
	Indoor Post-application	2	0.003	2.776	0.07

Human Equivalent Dose (HED) Calculation Method: ***HED = HEC x A x CF x ED x AF***

- HEC (Human Equivalent Concentration): Calculated exposure values for estimates of the concentration that would result in the same concentration to humans (mg/L).
- A (Adsorption): Ratio of absorption in respiratory tract compared to absorption by the oral route (100%) = **1.**
- CF (Conversion Factor): [(13.8L/min x 60min/hr) ÷ 70 kg] = **11.8 L/hr/kg**
- ED (Exposure Duration): Duration of daily human exposure = **Residential = 2hr/day and Occupational = 8hr/day**
- AF (Activity Factor): Animal default is **1**.

[1] Table adapted from D453658 (DeLeon, H., 26-AUG-2019); see reference for Agency's calculation methods and duration assumptions. HEC = Human Equivalent Concentration. HED = Human Equivalent Dose.

5.0 Dietary Exposure and Risk Assessment

5.1 Residues of Concern Summary and Rationale

The indoxacarb residues of concern concluded for plants, livestock, and drinking water are summarized in Table 5.1. The chemical name and structure of the indoxacarb residues of concern are provided in Appendix C of the supporting residue chemistry memorandum (D468389:TG00484551, E. Ford, 08-MAY-2024).

Table 5.1. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression[1]

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Indoxacarb and its R-enantiomer	Indoxacarb and its R-enantiomer
	Rotational Crop	Indoxacarb and its R-enantiomer	Indoxacarb and its R-enantiomer
Livestock	Ruminant	Indoxacarb and its R-enantiomer (for meat, meat byproducts, fat, and milk) Metabolite IN-MP819 (for milk only)[2]	Indoxacarb and its R-enantiomer
	Poultry	Indoxacarb, its R-enantiomer, and the metabolites IN-JT333, IN-JU873, IN-KB687, IN-KG433, IN-KT319, 5-HO-IN-JT333, and IN-VRN79[3,4]	Indoxacarb, its R-enantiomer, and the metabolites IN-JT333, IN-JU873, IN-KB687, IN-KG433, and IN-KT319
Drinking Water		Indoxacarb, its R-enantiomer, and the degradation products IN-JT333, IN-KG433, IN-KT413, and IN-ML437-0H	NA

[1] Adapted from: S. Levy, D325479, 09-MAR-2007; and D402100, C. Koper, 06-NOV-2012.
[2] Metabolite IN-MP819 was not determined in bovine feeding study. Ratio of metabolites of concern to measured residues (for milk only) is 1.8x (D339398, M. Sahafeyan, 23-MAY-2007).
[3] Metabolite IN-VRN79 (previously referred to as metabolite F) has been identified by NMR and LC/MS analysis; formula, C20H13ClF3N3O6 (D443744, D, Nadrchal, 01-MAR-2018),
[4] Metabolites 5-HO-IN-JT333 and IN-VRN79 were not determined in poultry feeding study. Ratio of metabolites of concern to measured residues in egg yolk, fat, muscle, liver, and skin were 1.8x, 2.8x, 1.5x, 2.5x, and 1.8x, respectively (D339398, M. Sahafeyan, 23-MAY-2007).

5.2 Food Residue Profile

Tolerances are established in the 40 CFR § 180.564 for the use of indoxacarb on a variety of crops, and in livestock to support uses in crops with associated feedstuff commodities. Magnitude of residue studies were submitted for coffee, strawberry, and sunflower. A review of the residue data submitted with the current petition is provided in D468389 (E. Ford, 08-MAY-2024). No deficiencies were noted in the submitted studies. Data analyses employed validated analytical methods and are supported by adequate storage stability data. Recommended tolerances are based on the newly acquired field trial data analyzed for the representative raw agricultural commodities (RACs). The proposed tolerances are not expected to raise the livestock dietary burden; therefore, the currently established livestock tolerances for indoxacarb remain appropriate. No additional residue chemistry data are required.

5.3 Water Residue Profile

The estimated drinking water concentrations used in the dietary risk assessment were provided by the Environmental Fate and Effects Divisions (EFED) (D455060, C. Koper, 23-JAN-2020) and incorporated directly into this dietary assessment; estimated drinking water concentrations (EDWCs) were not expected to change as a result of the proposed new uses (email communication with G. Orrick, 21-SEP-2023). The recommended maximum acute and chronic EDWCs for indoxacarb are 131 and 123 µg/L,

respectively; EDWCs are incorporated directly in DEEM-FCID for food categories "water, direct, all sources" and "water, indirect, all sources." EFED determined surface water concentrations using the Surface Water Concentration Calculator (SWCC) using an adjusted Percent Cropped Area (PCA) factor of 1.0. The EDWCs for ground water were estimated by the Pesticide Root Zone Model for Ground Water (PRZM-GW). EFED provided a time series distribution of water residues as a water residue distribution file (RDF) in support of the acute dietary analysis. These models and their descriptions are available at the EPA internet site: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/about-water-exposure-models-used-pesticide.

The EDWCs for indoxacarb and its metabolites of concern are summarized in Table 5.3.

Table 5.3. Summary of Estimated Surface Water and Groundwater Concentrations for Indoxacarb.[1]

Scenario	Surface Water Conc., ppb[2]	Groundwater Conc., ppb[3]
Acute	39	131
Chronic (non-cancer)	16	123
Chronic (cancer)	11	

[1] The estimated drinking water concentrations (EDWCs) used in the dietary risk assessment were provided by EFED (D455060, C. Koper, 23-JAN-2020). The previously calculated EDWCs are protective of the proposed new uses of indoxacarb.
[2] Calculated with the Surface Water Concentration Calculator (SWCC), values are adjusted with a Percent Cropped Area (PCA) factor of 1.0.
[3] Calculated with the Pesticide Root Zone Model for Ground Water (PRZM-GW). The post-breakthrough average concentration is recommended for chronic dietary assessment.

5.4 Dietary Risk Assessment

5.4.1 Description of Residue Data Used in Dietary Assessment

Partially-refined acute probabilistic and chronic dietary analyses were conducted by HED and are summarized in the corresponding dietary memo (D468390, E. Ford, 08-MAY-2024). Indoxacarb acute and chronic dietary exposure assessments were conducted using the DEEM-FCID Version 4.02. This software uses 2005-2010 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The 2005-2010 data are based on the reported consumption of individuals over two nonconsecutive survey days. For food commodities, residue distribution files (RDFs) were constructed from field trial residues for the probabilistic acute dietary assessment as appropriate, and average residues were computed for blended commodities and for the chronic dietary assessment. The EDWCs used in the dietary risk assessment were provided by the EFED (D455060, C. Koper, 23-JAN-2020) and are incorporated directly into this dietary assessment.

5.4.2 Percent Crop Treated Used in Dietary Assessment

The percent crop treated (%CT) estimates summarized in the BEAD screening level usage analysis (SLUA) Report for 2014-2023 (18-SEP-2023) are used for refinement of these dietary assessments.

For the acute dietary risk assessment, the following maximum %CT estimates are used: apples [15%]; apricots [15%]; broccoli [40%], cabbage [35%]; cauliflower [50%]; celery [10%]; cherries [2.5%]; corn [2.5%]; cotton [2.5%]; cucumbers [10%]; lettuce [15%]; nectarines [40%]; peaches [15%]; peanuts [5%]; peppers [20%]; plums/prunes [15%]; potatoes [2.5%]; pumpkins [2.5%]; soybeans [2.5%]; spinach [2.5%]; squash [10%]; sweet corn [5%]; tomatoes [15%]; and watermelons [2.5%].

For the chronic dietary assessment, the following average %CT estimates are used: apples [10%]; apricots [2.5%]; broccoli [30%], cabbage [20%]; cauliflower [25%]; celery [5%]; cherries [1%]; corn [1%]; cotton [1%]; cucumbers [2.5%]; lettuce [5%]; nectarines [30%]; peaches [10%]; peanuts [1%]; peppers [10%]; plums [5%]; potatoes [1%]; prunes [1%]; pumpkins [1%]; soybeans [1%]; spinach [1%]; squash [2.5%]; sweet corn [1%]; tomatoes [10%]; and watermelons [1%].

For all other crop commodities with indoxacarb uses and for the proposed new uses of indoxacarb, the assessment assumed that 100% of the crop was treated.

5.4.3 Acute Dietary Risk Assessment

For the general U.S. population and all population subgroups, acute dietary risk estimates are below HED's LOC (i.e., < 100% of the aPAD at the 99.9th percentile). Children (1-2 years old) are the most highly exposed population subgroup at 0.068039 mg/kg/day and 57% of the aPAD. The general US population exposure is 0.039189 mg/kg/day, occupying 33% of the aPAD.

5.4.4 Chronic Dietary Risk Assessment

For the US population and all population subgroups, chronic dietary risk estimates are below HED's LOC (i.e., < 100% of the cPAD). All Infants (< 1 year old) is the most highly exposed population subgroup at an exposure of 0.009989 mg/kg/day, occupying 50% of the cPAD. The general US population chronic exposure is 0.003073 mg/kg/day and occupies 15% of the cPAD.

5.4.5 Cancer Dietary Risk Assessment

A cancer dietary exposure and risk assessment was not conducted since indoxacarb is "not likely" to be carcinogenic to humans.

5.4.6 Summary Table

The results of the acute and chronic dietary exposure analyses are reported in Table 5.4.6.

Table 5.4.6. Summary of Dietary Food and Drinking Water Exposure and Risk for Indoxacarb.

Population Subgroup	Acute Dietary[1] (99.9th Percentile)		Chronic Dietary[2]	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.039189	33	0.003073	15
All Infants (< 1 year old)	0.055978	47	**0.009989**	**50**
Children 1-2 years old	**0.068039**	**57**	0.005163	26
Children 3-5 years old	0.047040	39	0.004043	20
Children 6-12 years old	0.041255	34	0.002802	14
Youth 13-19 years old	0.030007	25	0.002097	11
Adults 20-49 years old	0.026018	22	0.002915	15
Adults 50-99 years old	0.027970	23	0.003014	15
Females 13-49 years old	0.028051	23	0.002911	15

[1] Acute dietary analysis derived from a 0.12 mg/kg/day aPAD.
[2] Chronic dietary analysis derived from a 0.02 mg/kg/day cPAD.
[3] The most highly exposed population subgroups are written in **bold**.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

Residential (handler and post-application) exposures are not anticipated from the proposed new uses of indoxacarb. Therefore, quantitative residential handler and post-application risk assessments were not conducted in support of this action. However, there are currently registered uses of indoxacarb that may result in residential handler and post-application exposures. Those residential uses have been assessed previously in D453658 (H. DeLeon, 26-AUG-2019) and are not of concern. HED's residential risk estimate recommendations for use in aggregate human health risk assessment remain current and are summarized in Section 6.1.

6.1 Residential Risk Estimates for Use in Aggregate Assessment

There are no residential/non-occupational uses of indoxacarb proposed for the current action. HED has concluded the proposed new uses of indoxacarb do not affect the previous residential/non-occupational handler and post-application risk assessments summarized in the most recent human health risk assessment (D453658, H. DeLeon, 26-AUG-2019). Therefore, the recommendations for residential exposures used in the aggregate assessment remain current.

- The recommended short-term residential exposure for use in the child (1 to <2 years old) aggregate assessment is post-application incidental oral (hand to mouth) exposures resulting from spot (course/pin stream) applications to hard/carpeted surfaces.
- The recommended intermediate-/long-term residential exposure for use in the child (1 to <2 years old) aggregate assessment is incidental oral (hand to mouth) exposures from post-application exposure to treated pets (dogs).

Table 6.1 reflects the residential risk estimates that are recommended for use in the aggregate assessment for indoxacarb.

Table 6.1. Recommendations for the Residential Exposures for the Indoxacarb Aggregate Assessment.

Lifestage	Exposure Scenario	Dose (mg/kg/day)[1]				MOE[2]			
		Dermal	Inhalation	Oral	Total	Dermal	Inhalation	Oral	Total
Short-Term									
Children (1<2 yrs)	Spot (Coarse/Pin Stream) Carpet	N/A	N/A	0.012	**0.012**	N/A	N/A	170	**170**
Intermediate- and Long-Term									
Children (1<2 yrs)	Treated Pets (Dogs)	N/A	N/A	0.0028	**0.0028**	N/A	N/A	730	**730**

[1] N/A = not applicable. Total dose is the sum of dermal, inhalation, and incidental oral dose values.
[2] Total MOE = the MOEs associated with the highest residential doses: [LOC = 100].

The Agency notes the inhalation HEC selected for risk assessment is based on nasal portal of entry (POE) effects. Blood effects (hematological changes) were also seen in the 28-day inhalation study which is an identified endpoint (hemoglobin and red blood cells only at 6 months) for the WOE approach used to select the incidental oral POD. Typically, if the toxicological endpoints for exposure routes which may co-occur are the same these risk estimates would be combined. However, the HEC selected for inhalation assessment based on POE effects is lower than that calculated for the blood effects and is, therefore, protective of the potential blood effects. For the purpose of performing an

aggregate assessment, inhalation exposures based on POE effects should not be combined with background dietary (food and water) exposure based on use of the incidental oral POD. Therefore, the current adult inhalation exposure from residential handlers is not included in the aggregate assessment. For children 1 to <2 years old, only residential post-application incidental oral exposures are recommended for aggregate assessment.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. Based on the proposed and registered uses of indoxacarb, exposures can occur both from dietary sources (food and water) and in residential settings. However, since the inhalation and oral PODs are based on different toxic effects, and there is no dermal endpoint selected for indoxacarb, these exposures cannot be combined for aggregate risk assessment.

The aggregate risk assessments are intended to be representative of exposures that are likely to co-occur. The scenarios expected to result in the highest exposures are used as representative scenarios for the aggregate assessment and are considered protective of other scenarios. The lifestages selected for the aggregate assessments represent the population subgroups expected to be the most highly exposed for each scenario. For indoxacarb, the child lifestage with the highest dietary exposure (all infants <1 year old) does not match the child lifestage with the highest residential exposure (children 1 to <2 years old). The lifestages selected for each residential post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs[5]. This analysis provides a quantitative and qualitative basis for why children 1 to <2 years old are the representative lifestage for most residential post-application scenarios involving young children, as well as reasons why a residential assessment is not conducted for infants. For children, the indoxacarb aggregate assessment only combines the residential exposure estimates for children 1 to <2 years old with the dietary exposure estimates for that same lifestage, children 1-2 years old.

7.1 Acute Aggregate Risk

The acute aggregate risk estimates for indoxacarb includes food and drinking water only and are equivalent to the acute dietary risk estimates (Section 5.4.3), which are below HED's level of concern.

7.2 Short-Term Aggregate Risk

Because inhalation exposures cannot be combined with oral exposures, and there is no dermal endpoint selected for indoxacarb, a short-term aggregate assessment was not conducted for adults. The short-term aggregate risk for children includes background contribution from dietary (food and

[5] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

drinking water) exposure plus the short-term residential post-application exposures (incidental oral) from treated carpets.

For children, the short-term aggregate MOE is 120, which is above the LOC of 100 and not of concern.

Table 7.2. Short-Term Aggregate Risk Calculations.

Population	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Dietary Exposure mg/kg/day[3]	Residential Exposure mg/kg/day[4]	Total Exposure mg/kg/day[5]	Aggregate MOE (food, water, and residential)[6]
Children (1<2 yrs)	2.0	100	0.02	0.0052	0.012	0.017	120

[1] Level of Concern (LOC) = 100 (10X inter- and 10X intra- species uncertainty factors)
[2] Maximum Allowable Exposure (mg/kg/day) = NOAEL/LOC.
[3] Average Dietary Exposure = Chronic dietary exposure values for Children 1-2 years old. See Table 5.4.6.
[4] Residential Exposure = Incidental hand-to-mouth (HtM) oral exposure. See Table 6.1.
[5] Total Exposure = (Avg Food & Water Exposure + Residential Exposure).
[6] Aggregate MOE = [NOAEL/(Avg Food & Water Exposure + Residential Exposure)].

7.3 Intermediate-/Long-Term (Chronic) Aggregate Risk

Since there is no dermal hazard identified for indoxacarb and inhalation exposures cannot be aggregated with oral exposures due to differences in tox endpoints/PODs, the chronic aggregate risk for adults is equivalent to the chronic dietary risk and is not of concern.

For children (1 to <2 years old), the intermediate-/long-term (or chronic) aggregate risk for indoxacarb includes contribution from dietary (food and drinking water) exposure plus the intermediate-/long-term residential post-application exposure (incidental oral) to treated pets (dogs). For children, the intermediate-/long-term aggregate MOE is 250, which is above the LOC of 100 and not of concern.

Table 7.3. Intermediate-/Long-Term Aggregate Risk Calculations.

Population	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Dietary Exposure mg/kg/day[3]	Residential Exposure mg/kg/day[4]	Total Exposure mg/kg/day[5]	Aggregate MOE (food, water, and residential)[6]
Children (1<2 yrs)	2.0	100	0.02	0.0052	0.0028	0.0080	250

[1] Level of concern (LOC) = 100 (10X inter- and 10X intra- species uncertainty factors)
[2] Maximum Allowable Exposure (mg/kg/day) = NOAEL/LOC.
[3] Average Dietary Exposure = Chronic dietary exposure values for Children 1-2 years old. See Table 5.4.6.
[4] Residential Exposure = Incidental hand-to-mouth (HtM) oral exposure from Treated Pets – dogs. See Table 6.1.
[5] Total Exposure = (Avg Food & Water Exposure + Residential Exposure).
[6] Aggregate MOE = [NOAEL/(Avg Food & Water Exposure + Residential Exposure)].

7.4 Cancer Aggregate Risk

Indoxacarb is classified as "Not likely to be carcinogenic to humans;" therefore, cancer risks are not quantified.

8.0 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[6], 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).[7] 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 indoxacarb uses will be evaluated during the ongoing Registration Review process to ensure that all uses for that pesticide will be considered concurrently.

9.0 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[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 indoxacarb.

10.0 Cumulative Exposure/Risk Characterization

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to indoxacarb and any other substances and indoxacarb does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that indoxacarb has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common

[6] 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

[7] 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.

[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

mechanism groups (CMGs)[10] and conducting cumulative risk assessments (CRA)[11]. During Registration Review, the Agency will utilize this framework to determine if the available toxicological data for indoxacarb suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

11.0 Occupational Exposure/Risk Characterization

11.1 Short-/Intermediate-Term Occupational Handler Exposure and Risk Estimates

The agency uses the term handlers to describe those individuals who are involved in the pesticide application process. The agency 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, specified 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 summarized in Table 11.1. The occupational handler exposure and data assumptions are summarized in the supporting occupational risk assessment (TG00484551_ORE, H. DeLeon, 08-MAY-2024). The requested crop group expansions/conversion are covered by previous assessments and have not been reassessed here. A summary of the risk estimates for those uses is provided below.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

For the proposed new uses of indoxacarb, there are no inhalation risk estimates of concern (i.e., MOEs ≥ the LOC of 30) for occupational handlers wearing label specified baseline attire and no respirator; inhalation MOEs range from 65 to 120,000. No dermal hazard was identified for indoxacarb; therefore, quantitative dermal occupational handler exposure assessments were not conducted.

Occupational handler exposure and risk assessments for crops included in the crop group expansions/conversions were not conducted at this time as representative crop scenarios were assessed previously in D444002 (U. Hassan, 24-OCT-2017) and D438791 (U. Hassan, 22-JUN-2017). Since the use patterns, application rates, and equipment for these exposure scenarios remain unchanged, the previously-calculated occupational risk estimates for these scenarios remain current and are protective of the requested crop group expansions/conversions.[12] There are no occupational handler inhalation risks of concern (*i.e.,* MOEs ≥ the LOC of 30) identified for the requested crop group expansions/conversions of indoxacarb.

Note on flagger scenarios: The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for

[10] Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (USEPA, 1999)

[11] Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity (USEPA, 2002)

[12] See D444002 (U. Hassan, 24-OCT-2017) and D438791 (U. Hassan, 22-JUN-2017) for a detailed review of assessed occupational handler exposure scenarios, assessment parameters, and calculated risk estimates.

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 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Indoxacarb.						
Exposure Scenario	Crop or Target[1]	Inhalation Unit Exposure[2] (µg/lb ai) [PPE]	Maximum Application Rate[3] [Unit]	Area Treated or Amount Handled Daily[4]	Inhalation	
					Dose[5] (mg/kg/day)	MOE[6] [LOC=30]
Mixer/Loader						
Dry Flowable, Aerial, Broadcast	Orchard/Vineyard	8.96 [No-R]	0.11 [lb ai/acre]	350 acres	0.0043	65
	Field crop, typical			350 acres	0.0043	65
Dry Flowable, Airblast, Broadcast	Orchard/Vineyard	8.96 [No-R]	0.11 [lb ai/acre]	40 acres	0.00049	570
Dry Flowable, Chemigation, Broadcast	Field crop, typical	8.96 [No-R]	0.11 [lb ai/acre]	350 acres	0.0043	65
Dry Flowable, Groundboom, Broadcast	Orchard/Vineyard	8.96 [No-R]	0.11 [lb ai/acre]	40 acres	0.00049	570
	Field crop, typical acreage			80 acres	0.00099	280
Liquid, Aerial, Broadcast	Field crop, high-acreage	0.219 [No-R]	0.11 [lb ai/acre]	1,200 acres	0.00036	780
Liquid, Chemigation, Broadcast	Field crop, high-acreage	0.219 [No-R]	0.11 [lb ai/acre]	350 acres	0.00011	2,700
Liquid, Groundboom, Broadcast	Field crop, high-acreage	0.219 [No-R]	0.11 [lb ai/acre]	200 acres	0.000060	4,600
Applicator						
Spray (all starting formulations), Aerial, Broadcast	Orchard/Vineyard	0.0049 [EC/No-R]	0.11 [lb ai/acre]	350 acres	0.0000024	120,000
	Field crop, typical acreage			350 acres	0.0000024	120,000
	Field crop, high-acreage			1,200 acres	0.0000081	35,000
Spray (all starting formulations), Airblast, Broadcast	Orchard/Vineyard	4.71 [No-R]	0.11 [lb ai/acre]	40 acres	0.00026	1,100
Spray (all starting formulations), Groundboom, Broadcast	Orchard/Vineyard	0.34 [No-R]	0.11 [lb ai/acre]	40 acres	0.000019	15,000
	Field crop, typical acreage			80 acres	0.000037	7,500
	Field crop, high-acreage			200 acres	0.000094	3,000
Flagger						
Spray (all starting formulations), Aerial, Broadcast	Orchard/Vineyard	0.202 [No-R]	0.11 [lb ai/acre]	350 acres	0.000097	2,900
	Field crop, typical acreage					
	Field crop, high-acreage					
Mixer/Loader/Applicator						
Dry Flowable, Mechanically-pressurized Handgun, Broadcast (foliar)	Orchard/Vineyard	8.68 [No-R]	0.011 lb ai/gallon solution	1,000 [gallons solution]	0.0012	240
	Field crop, typical acreage					

[1] Crop/Target (formulation type): Typical acreage field crops include Strawberry (SG). High acreage field crops include Sunflower Crop Subgroup 20B (EC). Orchard crops include Coffee (SG).

[2] 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: EC = engineering controls; No-R = no respirator.

[3] Maximum Application Rate: Based on proposed label(s) (see Table 3.3).

[4] Area Treated or Amount Handled: Exposure Science Advisory Council Policy #9.2.

[5] 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).

[6] MOE: Inhalation MOE = Inhalation POD or HED (0.28 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 30.

11.2 Short-/Intermediate-Term Post-Application Exposure and 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.

11.2.1 Inhalation Post-Application Exposure and 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[13]. 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*[14]). 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 indoxacarb.

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.

Furthermore, inhalation exposure during dusty mechanical activities such as shaking and mechanical harvesting is another potential source of post-application inhalation exposure. However, the airblast applicator scenario is believed to represent a reasonable worst case surrogate estimate of post-application inhalation exposure during these dusty mechanical harvesting activities. The non-cancer inhalation risk estimate for commercial airblast application is not of concern (i.e., MOE ≥ LOC of 30).

11.2.2 Dermal Post-Application Exposures and Risk Estimates

No dermal hazard was identified for indoxacarb; therefore, quantitative dermal occupational post-application exposure assessments were not conducted for the proposed new uses and crop group

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

[14] Available online: Regulations.gov

expansion/conversion of indoxacarb.

Restricted Entry Interval: Indoxacarb is classified as Toxicity Category IV via the dermal route, Toxicity Category IV for skin irritation potential, and Toxicity Category IV for eye irritation potential. It is a skin sensitizer. A quantitative occupational post-application risk assessment was not conducted since a dermal POD was not selected for indoxacarb. 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] Worker Protection Statement interim REI of 12 hours is adequate to protect agricultural workers from post-application exposures to indoxacarb. HED would recommend the REI on the product labels be consistent with the WPS recommendations. This is the REI listed on the proposed labels and is considered protective of post-application exposure.

12.0 References

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D263986. Levy, S. (2000). Results of HED Metabolism Assessment Review Committee (MARC) Meeting of 6/12/00.

Appendix A. International Residue Limits Status Sheet.

(PC 067710)

Table A.1. Summary of U.S. and International Tolerances and Maximum Residue Limits for Indoxacarb

Residue Definition:

U.S. - 40 CFR 180.564 (a) (1):
Indoxacarb, (S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4][oxadiazine-4a(3H)-carboxylate, and its R-enantiomer, (R)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4][oxadiazine-4a(3H)-carboxylate

Canada - None

Codex - Sum of indoxacarb and its R enantiomer. The residue is fat soluble.

Commodity	*Tolerance (ppm)/Maximum Residue Limit (mg/kg)*			
	U.S.	Canada	Codex	Other[1]
Brassica, leafy greens, subgroup 4-16B	12	-	-	
Celtuce	14	-	-	
Chickpea, dry seed	0.2	-	Chick-pea (dry) - 0.2	
Coffee, green bean	0.03	-	-	
Cottonseed subgroup 20C	2	-	Cotton seed - 1	
Fennel, Florence, fresh leaves and stalk	14	-	-	
Field corn subgroup 15-22C	0.02	-	-	
Fruit, pome, group 11-10, except pear	1	-	Apple - 0.5	
Fruit, stone, group 12-12	1	-	Stone fruits (group) - 1	
Kohlrabi	12	-	-	
Leaf petiole vegetable subgroup 22B	14	-	-	
Leafy greens subgroup 4-16A	14	-	Lettuce, leaf - 3 Lettuce, head - 7	
Pear, Asian	0.2	-	Pear - 0.2	
Strawberry	4	-	-	
Sunflower subgroup 20C	1.5	-	-	
Sweet corn subgroup 15-22D	0.02	-	Sweet corn (corn-on-the-cob) - 0.02	
Vegetable, brassica, head and stem, group 5-16	12	-	Broccoli - 0.2 Cabbages, head - 3 Cauliflower - 0.2	
Vegetable, legume, bean, edible podded, subgroup 6-22A	0.9	-		
Vegetable, legume, bean, succulent shelled, subgroup 6-22C	0.9	-		
Vegetable, legume, pulse, bean, dried shelled, except soybean, subgroup 6-22E	0.2	-	Mung bean (dry) - 0.2 Cowpea (dry) - 0.1	
Vegetable, fruiting, group 8-10	0.5	-	Eggplant - 0.5 Peppers (subgroup) - 0.3 Tomato - 0.5	

Completed: E. Ford; 20-SEP-2023 using Global MRL

Appendix B. Physical/Chemical Properties

Table B.1. Physicochemical Properties of Indoxacarb		
Parameter	**Value**	**Reference**
Melting point/range	140-141°C	D244253, S. Levy, 19-JAN-2000
pH	5.32 at 25°C	
Density	1.34 at 20°C	
Water solubility	15.4 ± 2.3 ppb in pH 5 buffer 800 ppb (0.8 mg/L) at pH 7 (20°C)[1]	
Solvent solubility	1.72 g/L in n-heptane; 14.5 g/L in 1-octanol; 103 g/L in methanol; 117 g/L in o-xylene; 139 g/L in acetonitrile; 160 g/L in ethyl acetate; and >250 g/kg in methylene chloride, acetone, and dimethyl-formamide	
Vapor pressure (25°C)	2.5×10^{-8} Pa (1.9×10^{-10} mmHg)	
Dissociation constant, pK_a	Does not dissociate at pHs of 2.42-11.36	
Octanol/water partition coefficient, $Log(K_{OW})$	4.65 at pH 5	
UV/visible absorption spectrum	Molar absorptivities at three maxima were affected by pH, but not over wavelengths of environmental significance.	

[1] Table adapted from D402100, C. Koper, 06-NOV-2012

Appendix C. Review of Human Research

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 Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Agricultural Handler Exposure Task Force (AHETF) database; and the Outdoor Residential Exposure Task Force (ORETF) 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[15].

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