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WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: **Indoxacarb:** Preliminary Ecological Risk Assessment for Registration Review

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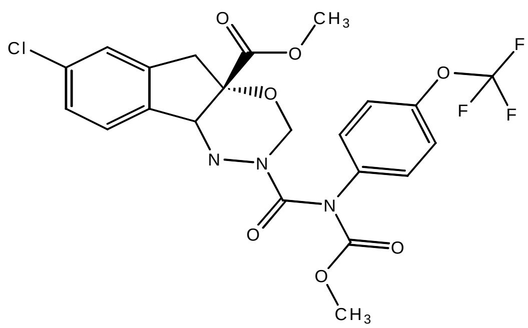
The Environmental Fate and Effects Division (EFED) has completed the preliminary risk assessment for the environmental fate, ecological risk, and drinking water exposure assessments to be conducted as part of the Registration Review of the insecticide indoxacarb (CAS 173584-44-6; PC Code 067710) and its degradates. The risk assessment is attached.

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Preliminary Environmental Fate and Ecological Risk Assessment in Support of Registration Review for Indoxacarb



CAS Number 173584-44-6

PC Code: 067710

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1.0 Executive Summary

Indoxacarb[1] was first registered in the United States in 2000 for the control of various lepidopteran pests on apples, pears, broccoli, cabbage, cauliflower, sweet corn, head and leaf lettuce, tomatoes, bell and non-bell peppers and cotton. Current labeled uses also include: alfalfa, peanuts, beans (including soybeans), root and tuber crops, herbs, beans, climbing and small vine fruits and berries, cranberries, cucurbits, and grapes. This assessment also considers the outdoor non-agricultural uses such as those on turfgrassess, fire ants, residential and commercial perimeter sprays, and ornamentals.

The technical formulation of indoxacarb has changed from a chemistry that once contained an enantiomer pair (DPX-MP062), with an insecticidally active *S*-enantiomer (*i.e.*, KN128) and inactive *R*-enantiomer (*i.e.*, KN127) (75% *S*-enantiomer and 25% *R*-enantiomer), to the current enriched technical formulation containing 95% of the *S*-enantiomer (DPX-JW062). It is this technical formulation that is assumed to be the material used to produce all current end-use products. The *R*-enantiomer has been considered less toxic in the past, however this may be true only for insects. In this assessment the R-enantiomer is considered a residue of concern for terrestrial and aquatic animals and plants, however because all formulated typical end-use products should be based on the new technical (based on communications from DOW Agrosciences) the exposure portion of this assessment assumes that the amount of active ingredient is in terms of the *S*-enantiomer and the approach taken accounts for all indoxacarb agricultural and non-agriculutural uses identified on the labels.

This assessment considers the most up to date toxicology and fate data, uses current exposure models including those exploring pathways not quantitatively assessed in past risk assessments, considers the most recent labels, incident information, and monitoring data. This preliminary environmental risk assessment addresses the re-evaluation of currently registered uses of indoxacarb.

The major routes of degradation for indoxacarb include alkaline-catalyzed hydrolysis and aqueous photolysis. Indoxacarb's low water solubility, high octanol/water partition coefficent (log K_{ow}) value, and relatively high soil sorption coefficient (K_{oc}) values suggest the tendency of the chemical to partition to soil and sediment; therefore, a low potential for leaching is expected. Batch equilibrium and aerobic soil metabolism studies conducted on the degradates IN-JT333 and IN-MP819 indicate that the degradates are less mobile and less persistent than parent indoxacarb. Microbial mediated degradation varied, with aerobic degradation occurring at a faster rate than anaerobic degradation.

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[1] S-methyl 7-chloro-2,5-dihydro-2-[[methoxycarbonyl) [4-(trifluromethoxy) phenylamino]carbonyl]indeno[1,2-e][1,3,4]oxadizine-4a(3*H*)-carboxylate; CAS Number 173584-44-6; PC Code: 067710

Indoxacarb's insecticidal mechanism of action involves blockage of the neuronal sodium channel. The insecticidal activity of indoxacarb is thought to be attributed to the rapid and extensive conversion of the (*S*) enantiomer KN128 to the more active metabolite IN-JT333 in insects. IN-JT333 has greater affinity for the sodium channel complex of insects than the parent compound. The major routes of degradation of indoxacarb include alkaline-catalyzed hydrolysis, photodegradation in water, and microbial mediated degradation. The conversion of indoxacarb parent to IN-JT333 is expected in soil and aquatic environments; therefore, there is potential effects to aquatic and terrestrial organisms.

Indoxacarb is highly toxic to terrestrial invertebrates and mammals on an acute basis, and shows some toxicity to birds. In aquatic toxicity tests, indoxacarb is highly toxic to fish and invertebrates. Two degradates have been identified (IN-JT333 and IN-MP819) as having substantially greater toxicity to some aquatic taxa, however this relationship varies across taxa. Chronic effects were observed for both freshwater and estuarine/marine fish (*e.g.,* growth, post-hatch survival). There is some uncertainty regarding the toxicity of parent and degradates to estuarine/marine fish, on an acute exposure basis: the available studies on the parent produced non-definitive endpoints, but chronic effects on survival were observed in a parent indoxacarb study and there are no available degradate chronic studies. Furthermore, direct comparisons of toxicity endpoints across chemicals is made difficult by missing data for some taxa. Chronic exposure to benthic invertebrates in toxicity tests suggests that indoxacarb is much more toxic to these taxa than the two degradates of concern. Indoxacarb is acutely toxic to birds and mammals, and is chronically toxic to mammals. In birds, the degradate IN-JT333 is of limited acute toxicity compared to the parent indoxacarb, but IN-JT333 is more acutely toxic to mammals than the parent; risk estimation for mammals relied upon IN-JT333 toxicity and exposure estimates. Indoxacarb and its degradates are highly toxic to honeybees on an acute oral and contact basis for adult honeybees, and acute and chronic basis for honeybee larvae. Several submitted Tier II honeybee toxicity studies were evaluated and the Agency determined that they were not suitable for quantitative use for various reasons (including having a single dose and not testing up to maximum labeled or estimated exposure rates). However, results of some these studies indicate that colony level effects may be occurring. Indoxacarb appears to be similarly toxic to bumblebee on an acute exposure basis. There is limited toxicity to terrestrial plants in the available studies, however these studies did not test to the highest application rate for the current labels. In aquatic plant studies, there is limited toxicity of indoxacarb or its degradates.

This assessment concludes that there are few mammalian acute risk concerns; however, there are extensive chronic concerns across all non-agricultural and agricultural uses and application rates modeled. There are many lines of evidence to indicate chronic risk for mammals including mean Kenaga values exceeding Levels of Concern (LOCs) and Estimated Exposure Concentrations (EECs) exceeding LOCs for long time durations. Aerial spray drift footprints for multiple indoxacarb applications extending out to 350 ft from the field, and concerns for small mammals consuming contaminanted fish were both a concern when modeling multiple season applications at the highest agricultural rate. For birds, there are acute risk concerns at all agricultural and non-agricultural application rates, but only chronic risk concerns at the greatest non-agricultural application rate of 1.437 lbs a.i./A for perimeter uses at commercial/industrial sites and at households/domestic dwellings. The drift footprint for avian LOCs was not a concern for agricultural areas, and EECs exceeded the LOC for a shorter time duration compared to mammals. For birds, there were only acute bioaccumulation concerns for sandpipers consuming contaminated fish with multiple season applications at the highest agricultural rate. Both acute and chronic risk concerns were identified to pollinators, however, the Tier II qualitative field studies were conducted below field rates and indicate mixed colony responses. Several highly pollinator attractive crops (*i.e.,* cotton and alfalfa) are registered for indoxacarb use and there was an incident involving a honeybee hive die-off on a cotton field. There are chronic risk concerns for all uses for benthic invertebrates, which based on the propensity for indoxacarb and the degradates of concern to partition to sediment, this conclusion is considered high confidence. Several uses have single or multiple season exceedances for water column invertebrates as well. However, there is less certainty in the risk conclusion because of the variability and uncertainty in the Toxic Equivalence (TEQ) estimation. There is a high confidence of low risk potential for fish, water column invertebrates, terrestrial plants and aquatic plants (

Table 1).

Table 1. Risk Summary Table for the Registered Uses of Indoxacarb

Exposure Duration	Risk Quotient Range	Risk to Non-Listed Species	Risk to Listed Species	Comments
Freshwater fish				
Acute	<LOC-0.05	No	Yes	Aerial and ground applications at 0.11 lbs a.i./acre, 3-day application interval have limited risk concerns.
Chronic	<LOC	No		None
Estuarine/Marine Fish				
Acute	<LOC-0.08	No	Yes	Arial, Chemigation, and ground applications at 0.11 lbs a.i./acre 3-day application interval and 5-day interval rate have limited risk concerns.
Chronic	None	No		N/A
Freshwater Invertebrates				
Acute	<LOC-0.05	No	Yes	Aerial and Ground exceedances at 0.11 lbs a.i./acre, 3-day application interval have limited risk concerns.

Exposure Duration	Risk Quotient Range	Risk to Non-Listed Species	Risk to Listed Species	Comments
Chronic	0.02-3.87	Yes	Yes	Aerial, Chemigation and Ground applications at 0.11 lbs a.i./acre, 3-day application interval, 5-day application interval for single and multiple seasons. Aerial and ground applications at 0.065 lbs a.i./acre have limited risk concerns.
Freshwater Benthic Invertebrates				
Acute	<LOC	No	No	N/A
Chronic	Porewater: 0.86-3.38 Sediment: 83.7-485.8	Yes	Yes	Aerial application exceedances for 0.11 lbs a.i./acre, 5-day application interval, 3 day-application interval and 0.11 lbs a.i./acre for a single season and 3-day application interval multiple seasons.
Estuarine/Marine Invertebrates				
Acute	<LOC-0.21	No	Yes	Aerial, chemigation and ground applications at 0.11 lbs a.i./acre; 3-day application interval for single and multiple seasons; Aerial, ground and chemigation applications 0.11 lbs a.i./acre, 5-day application interval; Perimeter treatments at 1.437 lbs a.i./acre
Chronic	None	No		N/A
Estuarine/Marine Benthic Invertebrates				
Acute	Not Assessed	No		Data insufficient to assess risk; however, freshwater benthic invertebrate conclusions are considered as a surrogate
Chronic	Not Assessed	Yes		
Mammals[2]				
Acute	Foliar Agricultural: 0.00-0.24	No	Yes	Majority of risk concerns for listed mammals at 0.1125 lbs a.i./A at a 3-day application interval with 4 applications.
	Foliar Non-Agricultural: 0.00-5.23	Yes		Acute risks at highest non-agricultural application rate for perimeter use.
	Granular[1]: 0.03-0.89			Mammal would have to consume 3.9 granules to exceed listed LOC.
	Contaminated Prey: 0.00-0.417	Yes	No	Acute Dose Based Risk for fog/water shrew, rice rat/star-nosed mole, small mink, large mink, small river otter, large river otter
Chronic	Foliar Agricultural: 0.08-468.3	Yes		Chronic effects at all application rates. Agricultural spray drift indicates LOC exceeded out to 348 feet for aerial applications at 0.1125 lbs a.i./A x 4 applications x 4 seasons.
	Foliar Non-Agricultural 0.08-468.3			
	Contaminated Prey: <LOC-7.24	Yes		Chronic dose based Risk for fog/water shrew, rice rat/star-nosed mole, small mink, large mink, small river otter, large river otter for multiple season

Exposure Duration	Risk Quotient Range	Risk to Non-Listed Species	Risk to Listed Species	Comments
				application only at the maximum agricultural rate (0.1125 lbs a.i./A)
Birds				
Acute	Foliar Agricultural: 0.00-1.60	Yes		Acute risks for listed and non-listed at all crop application rates modeled.
	Foliar Non-Agricultural: 0.00-34.83	Yes		Acute risks for listed and non-listed at all crop application rates modeled.
	Granular[1]: 0.04-3.34	Yes		A single bird would need to consume < 1 granule to exceed avian listed LOC.
	Contaminated Prey: <LOC-0.106	Yes		Acute risk concern for sandpipers consuming contaminated prey at the highest agricultural application rate 0.1125 lbs a.i./A x4 applications x 4 seasons.
Chronic	Foliar Agricultural: 0.00-0.87	No		No chronic risk concern.
	Foliar Non-Agricultural: 0.01-18.94	Yes		Chronic risk concern only at 1.437 lbs a.i./A application rate.
	Contaminated Prey: <LOC	No		No
Terrestrial Invertebrates				
Acute Adult-contact	1.49-57.1	Yes		Adult contact RQs exceed LOC for all scenarios.
Acute Adult-oral	0.04-226.3	Yes		Exceeds bee LOCs for all scenarios except the lowest non-agricultural application rate of 0.0375 lbs a.i./acre for soil application only.
Acute Larval-oral	0.01-1.08	Yes		Only exceeds honeybee LOC for the highest foliar non-agricultural rate of 1.437 lbs a.i./acre.
Chronic Adult-Oral	N/A	Uncertain		Chronic risk for adult honeybees in unknown. No chronic adult study submitted.
Chronic Larval-Oral	7.49-1162.9	Yes		Chronic larval RQs > LOC for all application scenarios.
Aquatic Plants				
N/A	<LOC	No		EECs are orders of magnitude less than the NOAECs.
Terrestrial Plants				

Exposure Duration	Risk Quotient Range	Risk to Non-Listed Species	Risk to Listed Species	Comments
N/A	<LOC	None		No risk up to the maximum tested dose. Risk unkown at concentrations between the highest test dose and the maximum application rate.

[1] The only granular form is the Adivon Fire Ant Granule.

[2] There are many lines of evidence to indicate chronic risk for mammals including mean Kenaga values exceeding Levels of Concern (LOCs) and Estimated Exposure Concentrations (EECs) exceeding LOCs for long time durations.

Note: NOAEC=No Observed Adverse Effect Concentration; EEC=Estimated Environmental Concentration; Chronic risk LOC = 1.0; Acute risk LOC for non-listed species = 0.5; Acute risk LOC for listed terrestrial animals = 0.1; Acute risk LOC for listed aquatic animals = 0.05; Aquatic and terrestrial plant risk LOC = 1.0; honeybee acute LOC=0.4 and honeybee chronic LOC=1.0.

2.0 Problem Formulation

The purpose of a problem formulation is to provide the foundation for the ecological risk assessment being conducted for the representative labeled uses of indoxacarb. A Registration Review Problem Formulation document was completed for indoxacarb in May of 2013 (USEPA, 2013a). The problem formulation identifies the ecosystems potentially at risk and assessment endpoints, and outlines a conceptual model which leads to the risk hypothesis evaluated in this assessment. The risk hypothesis written in the 2012 Registration Review Problem Formulation is summarized as follows: *Based on the application methods, mode of action, fate and transport, and the sensitivity of non-target aquatic and terrestrial species, indoxacarb has the potential to reduce survival, reproduction, and/or growth in non-target terrestrial and aquatic plants, aquatic fish and invertebrates, terrestrial invertebrates, as well as birds and mammals when used in accordance with the current labels. These non-target organisms include Federally-listed threatened and endangered species as well as non-listed species.*

2.1 Previous Assessments

Indoxacarb was first registered as a pesticide under the Federal Insecticide, Fungicide and Rodenticide Act in 2000 to control various lepidopteran pests on apples, pears, broccoli, cabbage, cauliflower, sweet corn, head and leaf lettuce, tomatoes, bell and non-bell peppers, and cotton. Subsequently EFED has conducted additional multiple ecological risk assessments for new uses of indoxacarb. The most recent assessment was conducted in 2016 (USEPA, 2016) to assess risks associated with DuPont's proposed label amendments for Avaunt® eVo; EPA Reg. No. 352-906. The amendment proposed an increased single application rate from 0.065 lb a.i./A to 0.11 lb a.i./A on succulent beans, brassica (cole), leafy green vegetables, leafy petioles, and spinach. The proposed label rate increase included 4 applications at 0.11 lb a.i./A for a maximum seasonal of 0.44 lb a.i./A, and maximum annual rates of 1.32 lb a.i./A (for 3 crop cycles of beans, brassica, sweet corn, fruiting vegetables/okra and spinach) and 1.76 lb a.i./A (for 4 crop cycles of leafy green vegetables and leafy petioles). The assessment concluded the following risks of concern:

- listed birds from acute exposure;
- listed and non-listed mammals from chronic exposure
- terrestrial invertebrates both larval (acute/chronic dietary) and adult (contact)
- listed freshwater fish from acute exposure
- listed estuarine/marine fish from acute exposure and non-listed estuarine/marine fish from chronic exposure;
- listed freshwater invertebrates from acute exposure; and
- listed and non-listed estuarine/marine invertebrates from acute and chronic exposure
- Risk to terrestrial plants from all proposed uses (presumed due to lack of toxicity data, the documented 'probable' plant incident involving indoxacarb, and effects seen on ryegrass emergence)

2.2 Updated Information Since the 2013 Problem Formulation

2.2.1 Ecological Effects Data

Previously Identified Data Gaps

Since the 2013 problem formulation and assessment, over 90 studies have been submitted to the US EPA. A suite of effects studies were identified as data gaps during the problem formulation (USEPA 2013) and in the 2016 Section 3 New Use Assessment. Since the time of the problem formulation, many data gaps have been addressed through the submission of data required by the DCI. However, no acceptable studies have been received to satisfy requirements for vascular aquatic plants, cold-water fish early life cycle and acute marine/estuarine fish toxicity endpoints (**Table 2**). These data gaps remain due to deficiencies with the studies submitted after the submission of the problem formulation and the Section 3 Risk Assessment (USEPA, 2016). EFED recommends submission of new studies to fulfill these data gaps and reduce uncertainty in the risk conclusion.

Table 2. Summary of the remaining data gaps for Indoxacarb

Guideline	Description	MRID	Classification	Comments	Data Gap Fulfilled?
850.4100 and 850.4150	Terrestrial plant Vegetative Vigor and Seedling Emergence	49551401-3 DPX-MP062 30WG and 150 EC	Supplemental	The submitted vegetative vigor and seedling emergence studies (MRID 49551402, 49551401, 49551403) were classified as supplemental quantitative because dose levels did not include the highest application rate (1.437 lbs a.i./acre). No effects were observed at the highest dose tested in any species for both dicots and monocots (0.12 lbs a.i./acre). Therefore, the NOAEC is set to the highest tested concentration. There is limited uncertainty in the current risk assessment regarding risk conclusions and rate tested in available studies.	**This data gap remains for applications between the highest dose tested and the maximum application rate.**
850.4400	Aquatic plant growth (aquatic vascular plant toxicity)	44477230 DPX-MP062	Supplemental	No. This study is scientifically sound but does not fulfill the guideline requirements for a Tier I aquatic plant toxicity test (*i.e.*, is classified as Supplemental). However, it is still useful for quantitative analyses. In the absence of additional data, the existing duckweed endpoints (*i.e.*, EC50 > 0.084 mg a.i./L; NOEC = 0.084 mg a.i./L) may be used to characterize the toxicity of indoxacarb to aquatic vascular plants.	US EPA has not received any additional aquatic vascular plant studies since the time of the problem formulation. **This data gap remains.**
850.1400	Fish early life stage (freshwater)	44477228 DPX-MP062	Supplemental	No. The submitted freshwater fish early life stage toxicity test is scientifically sound but does not fulfill the guideline requirements for a fish early life stage toxicity test (*i.e.*, is classified as Supplemental) due to the wide variability in measured concentrations and the limited number of replicates per dose to address the variability. However, it is still useful for quantitative purposes. In the	The USEPA has not received an acceptable coldwater fish species (rainbow trout) study since the time of the problem formulation, but there is an early life cycle test on the fathead minnow (warm water fish species) that is acceptable (MRID 49566208). **The data gap is only partially filled.**

Guideline	Description	MRID	Classification	Comments	Data Gap Fulfilled?
				absence of additional data, the existing early life stage endpoint (*i.e.*, NOEC = 0.15 mg a.i./L) may be used to characterize the toxicity of indoxacarb to freshwater fish from chronic exposure.	
850.1010	Acute toxicity freshwater invertebrates	44477221 IN-JT333	Supplemental	No. The study is scientifically sound but does not fulfill the guideline requirements for a freshwater invertebrate acute toxicity test (*i.e.*, is classified as Supplemental) because a definitive EC50 was not obtained. Five percent mortality (1 out of 20) was observed at the highest treatment concentration. However, it is still useful for quantitative analyses.	Since the problem formulation, the USEPA has received an acceptable acute toxicity freshwater invertebrate studies with definitive endpoints to use in risk assessment (MRID 46005801). **The data gap has been fulfilled since the problem formulation.**

Guideline	Description	MRID	Classification	Comments	Data Gap Fulfilled?
850.1075	Acute toxicity estuarine/marine fish	44477222 DPX-MP062	Supplemental	Yes. The study is scientifically sound but does not fulfill the guideline requirements for a freshwater fish estuarine/marine acute toxicity test (*i.e.*, is classified as Supplemental) because it did not test the chemical to its maximum solubility obtainable under brackish water conditions. In addition, 40% mortality and sublethal effects including erratic swimming and partial loss of equilibrium were observed at the highest treatment concentration, 0.37 mg a.i./L, resulting in a non-definitive endpoint (*i.e.*, LC50 > highest tested concentration). Based on guidance for using non-definitive endpoints, requesting additional data is recommended. In the absence of additional data, the conservative assumption of an LC50 of 0.37 mg a.i./L may be used for characterizing risk to estuarine/marine fish from acute exposure to parent indoxacarb.	The US EPA has not received any additional acute toxicity studies for marine/estuarine fish species since the problem formulation. The only available estuarine/marine fish toxicology studies are for the old technical formulation (DPX-MP062). **This data gap remains.**
Non-guideline	Chronic adult honeybee toxicity	None	None	N/A	No available chronic adult honeybee effects studies. Due to risk concerns identified in the acute contact and acute oral adult honeybee data and chronic larval data, these chronic adult honeybee toxicity data are important to a comprehensive risk assessment. **This data gap remains.**

Uncertainties

- There were no submitted effects studies available for chronic freshwater fish (degradates IN-MP819), acute and chronic estuarine marine fish (degradates IN- JT333 and IN-MP819), chronic freshwater invertebrates (IN-MP819 and IN-JT333), freshwater invertebrate acute sediment endpoints (degradates IN-JT333 and IN-MP819) and estuarine/marine invertebrates acute and chronic endpoints (degradates IN-JT333 and IN-MP819). Therefore, the risk conclusions for these particular species/degradate combinations are characterized with greater uncertainty. Acute to chronic ratios (ACR) were used to estimate endpoints. Risk conclusions could potentially change to the extent that toxicity estimates differ from the actual toxicity.

- The submitted vegetative vigor and seedling emergence studies (MRID 49551402, 49551401, 49551403) were classified as supplemental quantitative because dose levels did not include the highest application rate (1.437 lbs a.i./acre). No effects were observed at the highest dose tested in any species for both dicots and monocots (0.12 lbs a.i./acre). Therefore, the NOAEC is set to the highest tested concentration. There is limited uncertainty in the current risk assessment regarding risk conclusions and rate tested in available studies.

- There is a more sensitive endpoint from chronic mammalian studies. Hemolytic effects were observed at 8 mg/kg bw; however, this endpoint is not based on fecundity or reproductive success and was not evaluated quantitatively in this risk assessment. There is uncertainty regarding how hemolytic effects translate into survival and reproductive effects in wild mammals.

- There were no adult acute chronic honeybee data. Therefore, risk quotients could not be calculated and no risk determination could be made.

There are several assumptions and uncertainties associated with both the honeybee effects and exposure assessments for indoxacarb. While these assumptions and uncertainties are described in further detail throughout this assessment, a list of the major assumptions and uncertainties is provided below:

- The honey bee is a surrogate for assessing the responses of all species of bees to indoxacarb.
- Pollen and nectar are assumed to be the dominant routes of exposure for bees.
- Model estimated exposure concentrations (EECs) serve as a conservative estimate for predicting exposure to individual adult and larval honey bees resulting from foliar, soil, and injection applications and, therefore, may over-estimate exposure.
- It is assumed that pollen and nectar are equally potent routes of exposure when assessing the risk to individual bees.
- Extrapolation of individual bee risk findings to risks at the colony-level is uncertain due to the complexities of exposure and effects at the colony level.

- Off-field estimates of risk are based on modeled exposure estimates which cannot be refined with available residue data and are assumed to be to pollinator friendly crops at the time of bloom. Therefore, potential off-field risks may be overestimated.
- Available data from crop residue studies may not fully capture variation in temporal and spatial factors (*e.g.*, weather patterns, soil type) that affect indoxacarb residues in pollen and nectar for the tested crop.
- Tier II honeybee studies were not conducted at the maximum field rate tested; thus, there is a moderate degree of uncertainty in characterizing potential risk at the colony level. Several tunnel and feeding studies were voluntarily submitted with varied quantitative value, but risk cannot be precluded.
- Chronic adult honeybee studies were not conducted; thus, chronic effects are uncertain and risk is unable to be precluded.

Updated Requirements since the Problem Formulation

Based on the new Pollinator Risk Assessment Framework[2], additional studies were submitted for indoxacarb since the Problem Formulation and last risk assessment.

- Non-guideline (OECD 237) - Acute oral toxicity to larval honeybees
- Chronic oral toxicity to larval honeybees
- Residues in pollen and nectar (if risk concerns are identified based on Tier I toxicity studies)
- Semi-field and full-field studies (if risk concerns are identified based on lower tier studies)

2.2.2 Environmental Fate Data

Several environmental fate studies conducted with indoxacarb or its degradates IN-JT333 and IN-MP819 were submitted to the Agency since 2013 (**Table 3**). All studies were classified as acceptable or supplemental and are used in this risk assessment.

Data Gaps

- One anaerobic soil metabolism (835.4200) study has been submitted. OCSPP guidance recommends that these tests be performed with four soils. Although this study is not used in the aquatic exposure modeling, the data will inform anaerobic degradation in terrestrial environments.
- A storage stability in water is required under 40 CFR part 158 for terrestrial outdoor uses. This study will inform chemical stability in aqueous environments.

[2]http://www2.epa.gov/sites/production/files/201406/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

Table 3. Summary of Submitted Environmental Fate Studies for Indoxacarb and its degradates

Guideline	Description	MRID	Classification	Data Gap?	Additional Data Recommended for Request? (Risk Management Recommendations)
835.2120 161-1	Hydrolysis	44477301 45795801 49577705	Supplemental Acceptable Supplemental	No	--
835.2240 161-2	Photodegradation in Water	44477302 45795802	Supplemental Acceptable	No	--
835.2410 161-3	Photodegradation in Soil	44477303	Supplemental	No	--
835.4100 162-1	Aerobic Soil Metabolism	45166303 44477304 44477307 45795812 45850001 45906701 45795803 49577706 49912201	Supplemental Marginally Acceptable Supplemental Supplemental Supplemental Acceptable [1] Acceptable [2] Acceptable [5] Acceptable [6]	No	--
835.4200 162-2	Anaerobic Soil Metabolism	49577707	Supplemental	Yes	Yes. One anaerobic soil study has been submitted. OCSPP guidance recommends that these tests be performed with four soils to inform anaerobic degradation in terrestrial environments.
835.4300 162-4	Aerobic Aquatic Metabolism	45793301 44477306 49577708	Marginally Acceptable Supplemental Supplemental	No	--
835.4400 162-3	Anaerobic Aquatic Metabolism	45795804 44477305	Supplemental Supplemental	No	--
835.1230	Adsorption/ Desorption	45795809 49912202	Supplemental[3] Supplemental[7]	No	--
835.1240 163-1	Leaching	44477309	Supplemental	No	--
835.6100 164-1	Terrestrial Field Dissipation	45850002	Supplemental[4]	No	--
		46780201	Supplemental	No	--
		49577701	Supplemental	No	--
		49577702	Supplemental	No	--
		49577703	Supplemental	No	--
		49577704	Supplemental	No	--

Guideline	Description	MRID	Classification	Data Gap?	Additional Data Recommended for Request? (Risk Management Recommendations)
	Storage Stability in Soil	49599601	Acceptable	No	--
	ECM/ILV in Soil and Sediment	49599603 49623401 49934101	Supplemental	No	--
	Storage Stability in Water	--	--	Yes	Yes. Storage stability in water is required under 40 CFR part 158 for terrestrial outdoor uses (part of Terrestrial Field Dissipation study)
	ECM/ILV in Water	49599604 49599606	Acceptable	No	--
165-4	Bioaccumulation in Fish (BCF)	45805301	Acceptable	No	--

[1] Acceptable with MRID 45795803 and MRID 44477304
[2] Acceptable with MRID 44477304
[3] Classified Supplemental together with study MRID 44477308
[4] Classified Supplemental together with studies MRID 44477312, 44477315, 44477316
[5] Aerobic soil metabolism study conducted with the degradate IN-JT333.
[6] Aerobic soil metabolism study conducted with the degradate IN-MP819.
[7] Batch equilibrium study conducted with the degradate IN-MP819.

3.0 Use Characterization and Methods of Application

Indoxacarb is formulated as a suspension concentrate and water-dispersible granule as well as multiple types of bait for nonagricultural use. There are two formulations of indoxacarb registered for agricultural use on crops and several types of formulations for use in bait stations or gels. Agricultural uses include foliar sprays that are applied via broadcast, chemigation and aerial methods. Registered agricultural uses of indoxacarb are provided in **Table 4.** A 2017 Label Data Report by the Biological and Economic Analysis Division (BEAD) provides application rates for all registered uses of indoxacarb. For agricultural uses, the single application rates range from 0.0656 lb a.i./A to 0.1125 lb a.i./A, with two to four applications allowed per crop cycle for a maximum application rate of 0.22 to 0.45 lb a.i./A/crop cycle. Application intervals range from 3 to 21 days for agricultural crops. The maximum seasonal application rate of indoxacarb is 0.44 lbs a.i./A (4 applications at 0.11 lbs a.i./A) for all crops.

Non-agricultural application methods consist of mound treatment, perimeter treatment, bait application, gel treatment, spot treatment, crack and crevice treatment, granular bait application, outdoor general surface spray, high volume spray, and spot-on treatment (for dogs and cats) (**See Appendix B).** The lowest application rate for non-agricultural uses is a foliar application spray with a single application rate of 0.0375 lbs a.i./Acre per year, for use on commercial/industrial premises and equipment, recreational areas, households, domestic dwellings, non-agricultural uncultivated areas/soils and golf course turf. The single maximum application rate for non-agricultural uses is for foliar spray at 1.437 lbs a.i./A for use on commercial/industrial premises/equipment, household domestic dwellings and refuse and solidwaste sites. Indoxacarb also has uses on ornamental lawns and turn at a single maximum application rate of 0.225 lbs a.i./A.

Table 4. Agricultural Uses of Indoxacarb

Uses	Single Maximum App. Rate (lb a.i./ acre)	Applications Per Season	Minimum Application Interval (d)	Maximum Annual Application Rate (lb a.i./ Acre/Year)	Multiple Season Crop Cylces Allowed[1]?	Application Method
DuPont Avaunt Insecticide 352-597						
Small fruit vine climbing subgroup, expect fuzzy kiwi fruit	0.1125	2	21	0.225	No	Broadcast Ground/Aerial
Beans (Dried Type)	0.1125	4	7	1.35	Multiple	Broadcast Ground/Aerial
Beans (Succulent, except soybean)	0.1125	NS	7	1.05	Multiple	Broadcast Ground/Aerial
Beets (unspecified)	0.1125	4	3	1.8	Multiple	Broadcast Ground/Aerial
Brassica (head & stem vegetables)	0.065625	4	3	1.05	Multiple	Broadcast Ground/Aerial
Bushberries	0.1125	4	7	0.45	No	Broadcast Ground/Aerial
Sweet Corn	0.06525	4	3	0.7875	Multiple	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Highbush Cranberry	0.1125	3	7	NS	No	Broadcast Ground/Aerial
Cucurbit Vegetables	0.1125	4	5	1.35	Multiple	Broadcast Ground/Aerial
Grapes	0.1125	2	21	0.225	No	Broadcast Ground/Aerial
Leafy Greens	0.1125	4	3	1.8	Multiple	Broadcast Ground/Aerial
Leafy Vegetables	0.065625	4	3	1.05	Multiple	Broadcast Ground/Aerial
Low growing berries	0.1125	3	7	NS	No	Broadcast Ground/Aerial
Mint/Peppermint/ Spearmint	0.06525	4	3	0.2625	No	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Okra	0.06525	4	5	0.7875	Multiple	Broadcast Ground/Aerial
Pear	0.1125	4	7	0.045	No	Broadcast Ground/Aerial
Pome fruit	0.1125	4	7	0.45	No	Broadcast Ground/Aerial
Potato (white/Irish or unspecified)	0.1125	4	5	1.8	Multiple	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation

Uses	Single Maximum App. Rate (lb a.i./ acre)	Applications Per Season	Minimum Application Interval (d)	Maximum Annual Application Rate (lb a.i./ Acre/Year)	Multiple Season Crop Cylces Allowed[1]?	Application Method
Root & Tuber vegetables	0.1125	4	5	1.8	Multiple	Broadcast Ground/Aerial
Spinach	0.06525	4	3	1.05	Multiple	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Stone fruits	0.1125	4	7	0.45	No	Broadcast Ground/Aerial
Steward Insecticide 352-598						
Alfalfa	0.110854	NS	5	NS	No	Broadcast Ground/Aerial
Peanuts (unspecified)	0.110854	NS	5	NS	No	Broadcast Aerial Broadcast Ground
Soybeans (unspecified)	0.110854	NS	5	NS	No	Broadcast Ground/Aerial
DuPont Steward EC Insecticide 352-638						
Alfalfa	0.110513	NS	5	0.44	No	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Beans (dried type)	0.110513	4	7	0.44	No	Broadcast Ground/Aerial
Cotton	0.1105135 8	4	5	0.44	No	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Peanuts (unspecified)	0.110513	4	5	0.04400	No	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation
Soybeans (unspecified)	0.110513	4	5	0.4400	No	Broadcast Ground/Aerial Chemigation/Overhead sprinkler irrigation

NS=Information not provided on label or LUIS report, where applicable information from other labels was used in modeling.

[1]Multiple Seasons determined if the maximum annual application rate is four times greater than the single maximum application rate times the number of applications and also from (USEPA, 2016)

The results of a Screening Level Usage Analysis (SLUA) for indoxacarb by BEAD are provided in **Table 5.** The use of minor/speciality crops is not captured in the SLUA. This analysis lists agricultural uses of indoxacarb in terms of estimated total pounds of active ingredient. SLUA data sources include:

- USDA-NASS (United States Department of Agriculture's National Agricultural Statistics Service)
- Private Pesticide Market Research
- California DPR (Department of Pesticide Regulation)

The top 3 agricultural uses of indoxacarb from 2005 to 2015 in terms of pounds of a.i. applied were alfalfa, cotton and tomatoes.

Table 5. Screening Level Estimates of Agricultural Uses of Indoxacarb – Reporting Time: 2005-2015

Crop		Average Lbs. A.I. Applied Annually	Percent Crop Treated	
			Average	Maximum
1	Alfalfa	10,000	<2.5	<2.5
2	Apples	2,000	5	10
3	Apricots	<500	5	15
4	Blueberries	<500	5	5
5	Broccoli	4,000	45	70
6	Brussels Sprouts *	<500	40	70
7	Cabbage	1,000	20	35
8	Cantaloupes	<500	5	10
9	Cauliflower	1,000	35	60
10	Celery	<500	5	5
11	Cherries	<500	<2.5	<2.5
12	Cotton	9,000	<2.5	<2.5
13	Cucumbers	1,000	<2.5	10
14	Grapes	<500	<2.5	5
15	Lettuce	2,000	5	15
16	Nectarines	1,000	15	15
17	Peaches	1,000	<2.5	10
18	Peanuts	4,000	5	10
19	Pears	<500	<1	<2.5
20	Peppers	1,000	15	30
21	Plums/Prunes	<500	5	5
22	Potatoes	1,000	<2.5	<2.5
23	Pumpkins	<500	<2.5	<2.5
24	Soybeans	6,000	<1	<2.5
25	Spinach	<500	<2.5	5
26	Squash	<500	<2.5	5
27	Sweet Corn	1,000	<2.5	10
28	Tomatoes	7,000	20	40
29	Watermelons	<500	5	10

All numbers rounded.
<500: less than 500 pounds of active ingredients.
<2.5: less than 2.5 percent of crop is treated.
<1: less than 1 percent of crop is treated.

* Based on CA DPR data only (80% or more of U.S. acres grown are in California).
Note: These results reflect amalgamated data developed by the Agency and are releasable to the public.

Another measure of usage is the use intensity. For the purposes of this assessment, use intensity is expressed as pounds a.i. applied per square mile for agricultural crops (non-agricultural uses are not included in the database). This differs from the application rate, which is expressed as the pounds a.i. applied per treated acre. The USGS pesticide usage data maps in **Figure 1** illustrate the national agricultural indoxacarb usage at the Crop Reporting District (CRD) level and spatially represents indoxacarb use intensity in the US.

The usage estimates from USGS are based on private market surveys of pesticide use in agriculture. They are intended for broad-scale assessments such as at the national or regional level, and are not suitable for sub-state quantitative analyses. This is because the survey data are limited to the states that represent the top 80-90 percent of acreage for the individual crops; therefore, use may be occurring in regions outside the scope of the survey. CRDs showing no usage of pesticides may be due to either the lack of pesticide use in the region or non-participation in the agricultural surveys. In addition, across the years, there may be variations in the specific crops included in the CRD survey. This may result in a lower annual average for the CRD. Therefore, this assessment uses these data for qualitative purposes only, in the form of the maps below, to provide a geographic footprint of a pesticide's use. Nationwide, the use of indoxacarb is mostly applied to alfalfa, vegetables, and fruit (**Figure 2),** which are highly attractive to bees and may be of concern.

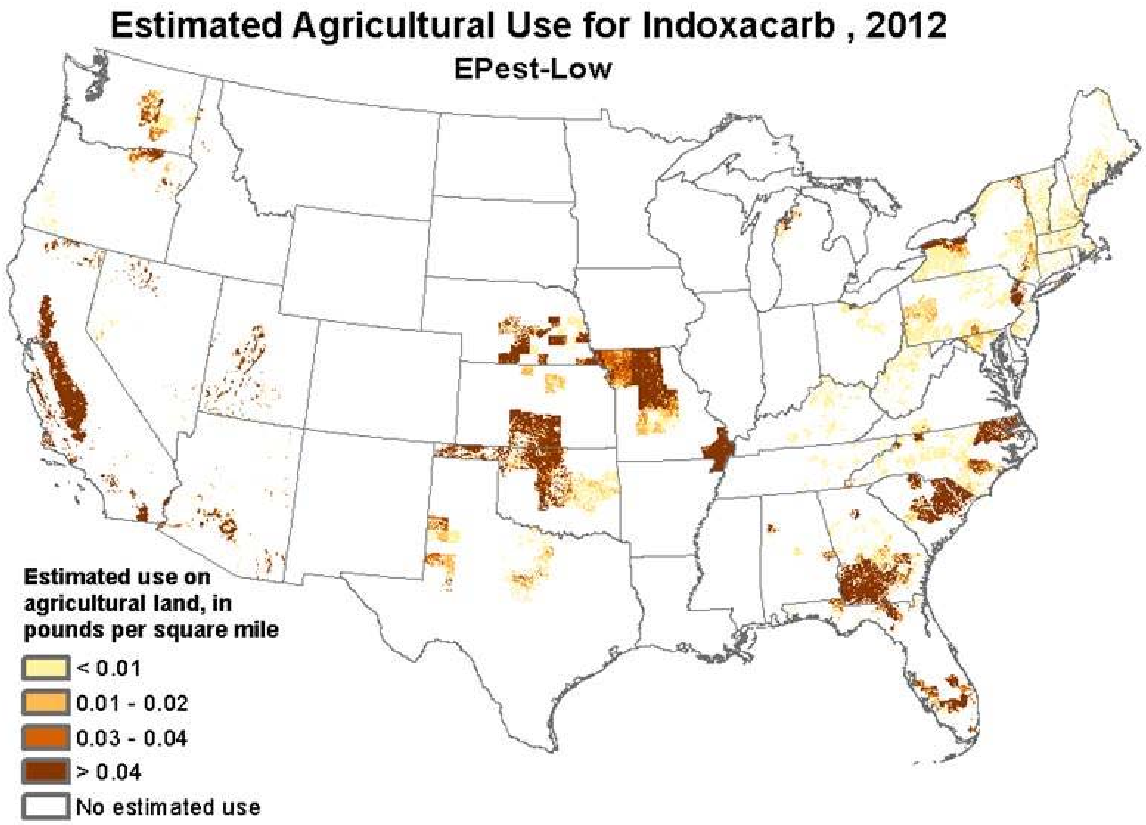


Figure 1. Estimated Agricultural Use of Indoxacarb in The United States, 2012. (Source: USGS, Accessed May 2017 at https://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2012&map=INDOXACARB&hilo=L)

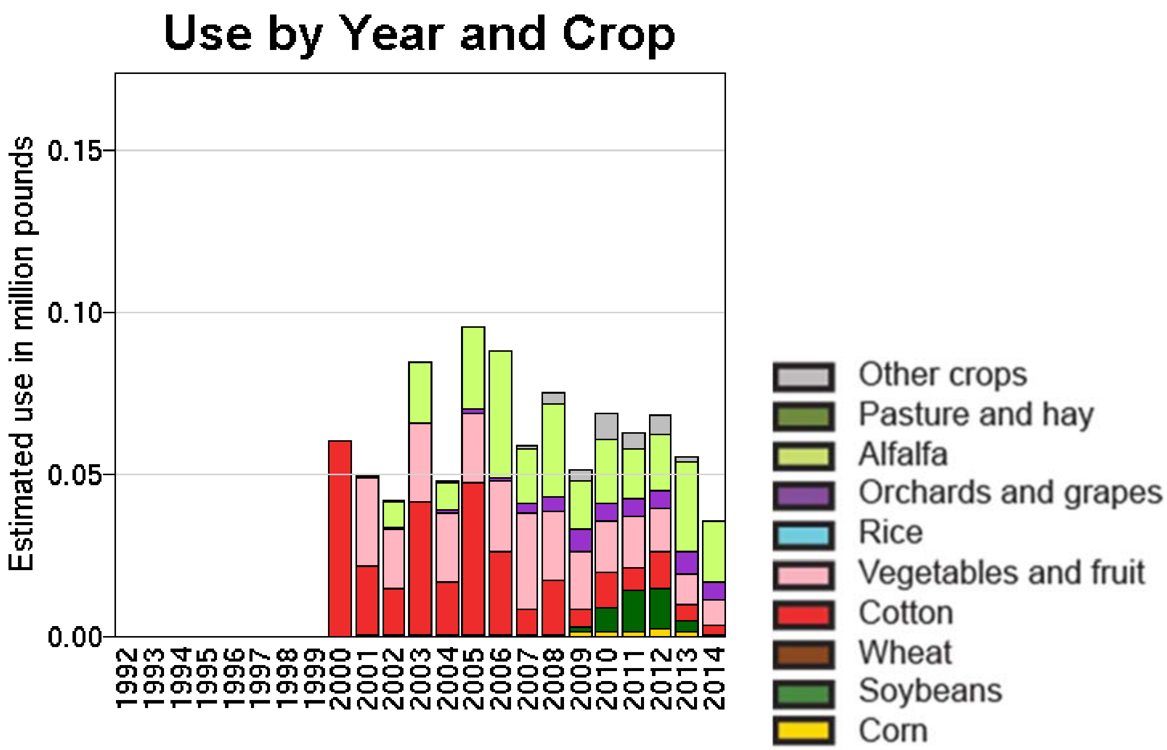


Figure 2. Indoxacarb Agricultural Use by Year and Crop. (Source, USGS Accessed May 2017 at https://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2012&map=INDOXACARB&hilo=L)

4.0 Environmental Fate and Transport

4.1 Indoxacarb

The major routes of degradation for indoxacarb include alkaline-catalyzed hydrolysis and aqueous photolysis. Indoxacarb's water solubility (0.8 mg/L), log Kow value (4.65), and Koc values (mean Koc = 5125 mL/$g_{o.c.}$) suggest the tendency of the chemical to partition to soil and sediment; therefore, a low potential for leaching is expected.

Indoxacarb has a low potential to volatilize under dry conditions considering the chemical's vapor pressure (1.9×10^{-10} mm Hg at 25ºC; MRID 44477109). Calculated Henry's Law constant (1.6×10^{-10} atm*m^3/mol) indicates non-volatility from water. Plant and soil volatility studies indicate that indoxacarb has low volatility from plant and soil surfaces with less than 3% of applied radioactivity volatilizing from lettuce plants and soil surface. Hydrolysis is an important degradation route in an alkaline aqueous environment. Indoxacarb undergoes alkaline-catalyzed hydrolysis with hydrolysis increasing with increasing pH. Half-lives (90th percentiles) decrease from 639 days at pH 5 to 36 days at pH 7 and 1 day at pH 9 (MRID 44477301, 45795801, 49577705).

Photodegradation is a potential degradation pathway in clear, shallow surface waters. Aqueous photolysis studies show phototransformation half-lives of 3.16 and 5 days (MRID 44477302, 45795802). Indoxacarb was stable to soil photolysis (MRID 44477303).

Indoxacarb's persistence[3] in soil and sediment-water systems varied depending on environmental conditions. Aerobic soil metabolism half-lives ranged from 3 to 693 days; however, indoxacarb is persistent in only one (Chino) soil ($t_{1/2}$= 693 days; MRID 45166303) while six other soil half-lives ranged from 3 to 30 days. The slow degradation rate in the Chino soil (MRID 45166303) is likely an aberration, due to microbial inactivity owing to the soil's fallow and frequently flooded conditions before testing. This soil was microbially active, as determined by viability tests at study initiation and termination, and did not differ dramatically from the other test soils on the characterization parameters typically predictive of degradation potential (i.e., pH, % organic matter, cation exchange capacity).

A single anaerobic soil metabolism study was conducted with a calculated half-life of 10.5 days (MRID 49577707). Aerobic aquatic metabolism half-lives ranged from 3 to 58 days while anaerobic aquatic system half-lives were more persistent with half-lives ranging from 147 to 315 days.

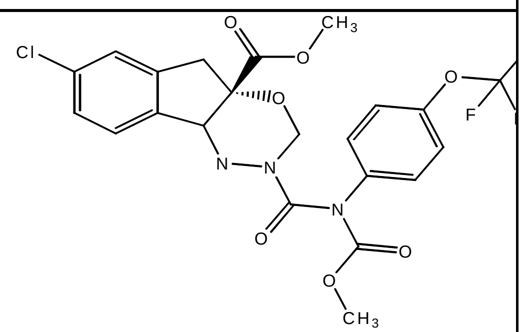
In terrestrial field dissipation (TFD) studies, indoxacarb dissipated with DT_{50}s ranging from 7 to 119 days. These dissipation results were relatively comparable to laboratory aerobic soil metabolism half-lives. TFD studies showed some movement of parent and residues but were contained in the upper soil horizons. The major degradate IN-KT413 formed up to 19.6% (**Appendix C**) but was was not detected in soils below 50 cm (20 inches).

Indoxacarb shows bioconcentration potential in fish with calculated fish bioconcentration factors (BCF) of 1044-1351X in whole fish tissues with the depuration half-life occurring at less than 10 days (MRID 44477319, 45805301). The high BCF and rapid depuration suggest is that indoxacarb metabolism and excretion of the compound does occur but the potential for magnification up the food chain appears to be limited, and the concentration in fish will be susceptible to changes in the water concentration.

Table 6. shows the available environmental fate and transport data of indoxacarb with MRID references.

[3] http://www.pbtprofiler.net/criteria.asp

Table 6. Physical and Chemical Properties of Indoxacarb

Parameter	Value	Source/MRID #
Common name	Indoxacarb (active *S*-enantiomer)	
CAS number	173584-44-6	
Chemical name	Methyl 7-chloro-2,5-dihydro-2 [[(methoxycarbonyl)[4(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylate	
Chemical Class/Category	Oxadiazine insecticide	
Empirical formula	$C_{22}H_{17}ClF_3N_3O_7$	
Structure (active *S* enantiomer)		Product Chemistry Data
Molecular Mass	527.8 g/mole	
Water Solubility	0.8 mg/L at 20°C	
Vapor pressure (25°C)	1.9×10^{-10} mm Hg	
Henry's Law Constant	1.6×10^{-10} atm m^3/mol	Calculated[1]
Octanol/water partition coefficient (K_{ow})	44,668 (log Kow = 4.65)	Product Chemistry
Dissociation Constant (pKa)	No ionization at any environmentally-relevant pH	Product Chemistry
Hydrolysis ($t_{1/2}$)	pH 5 = 519, 578 days pH 7 = 38, 21.8, 17.4 days pH 9 = 1, 1.11days	44477301 45795801 49577705
Aqueous Photolysis ($t_{1/2}$) (pH 5)	3.16 days 5.0 days	44477302 45795802

Parameter	Value	Source/MRID #
Soil Photolysis	stable	44477303
Aerobic Soil Metabolism ($t_{1/2}$ at 25 C)	3 days	44477304
	3 days	44477307
	6 days	45850001
	27 days	45166303
	10 days	45166303
	30 days	45166303
	693 days	45166303
Anaerobic Soil Metabolism ($t_{1/2}$)	10.5	49577707
Aerobic Aquatic Metabolism ($t_{1/2}$ at 20C)	30.7 days	45793301
	39.8 days	45793301
	38.1 days	45793301
	21.3 days	45793301
	52.0 days	44477306
	58.0 days	44477306
	36.0 days	44477306
	42.0 days	44477306
	3.28 days	49577708
	5.37 days	49577708
Anaerobic Aquatic Metabolism ($t_{1/2}$ at 20C)	192.5 days	45795804
	315.1 days	45795804
	147.0 days	44477305
	231.0 days	44477305
Soil Partition Coefficient (K_{OC}) (mL/$g_{O.C.}$)	5100	45795809
	3300	
	9600	
	2500	
Terrestrial Field Dissipation (DT_{50})	72 - 79 days (FL, CA bare sand)	44477312, 44477315, 44477316

Parameter	Value	Source/MRID #
	29-113 days (DE, TX bare ground)	44477311
	73-119 days (CA, FL bare ground)	45850002
	53.6 days (NC turf plot)	46780201
	9.84 days (France, bare ground)	49577701
	7.48 days (Spain, bare ground)	49577702
	9.33 days (Italy, bare ground)	49577703
	8.23 days (Germany, bare ground)	49577704
Bioconcentration in Bluegill Sunfish (BCF)	395 to 504X in edible tissues 1568 to 2081X for non-edible tissues 1044 to 1351X for whole fish	44477319 45805301

[1] = Henry's Law (atm-m^3/mole) = (VAPR/760)/(SOL/MWT), where VAPR is vapor pressure in torr, MWT is molecular weight in g/mol, and SOL is the solubility in water in mg/L.

The technical formulation of indoxacarb has changed over time from its original composition of a 75:25 percent mixture of *S* and *R* enantiomers to an enriched technical containing 95% of the *S*-enantiomer. The R-enantiomer has been considered less toxic in the past, and at this time is not considered a residue of concern because all formulated typical end-use products should be based on the new technical and thus primarily be the *S*-enantiomer. Additionally, the *S*-enantiomer has been identified as the active ingredient on the registrant-submitted labels. The environmental fate data can be bridged for the parent indoxacarb because there was no enantioselective degradation found in the soil and aquatic metabolism studies.**Table 7** provides a list of the chemical common names that are discussed in this assessment, as well as a list of chemical synonyms that have been used in registrant submitted studies.

Table 7. Common chemical names, synonyms referred to in studies and full chemical names of indoxacarb and its degradates

Chemical Common Name	Synonym in Submitted Studies	Comment	IUPAC Chemical Name	Molecular Weight	Residue of Concern for Aquatic Assessment?
Current Technical Formulation (Refined *S*-Enantiomer)					
Indoxacarb	DPX-JW062; DPX-KN128	95% *S*-Enantiomer (*R*-Enantiomer quantity unknown)	Methyl 7-chloro-2,S-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[l,2-e][l,3,4]oxadiazine-4a(3H)-carboxylate	527.84 g/mol	Yes
Old Technical Formulation (Mixture of *S* and *R* Enantiomers)					
DPX-MP062	75% *S* 25% *R* mixture; DPX-MP062;	Technical Mixture: 79% *S* (KN128) and 21% *R* (KN127) (94.5% purity for mixuture)	(*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	527.84 g/mole	Yes
Degradates of *S*-enantiomer (KN128)					
DPX-KN125		Degradate of *S* Enantiomer	7-Chloro-2,5-dihydro-2-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]-, methyl ester, (4aS)-indeno[1,2-e] [1,3,4]oxadiazine-4a(3//)-carboxylic acid	469.8 g/mole	
IN-JT333		Degradate	methyl-7-chloro-2,5-dihydro -2-[[[4(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine-4a(3H)-carboxylate	469.81 g/mol	Yes
IN-KG433		Degradate	Methyl-5-chloro-2,3-dihydro-2-hydroxy-1[[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]hydrazono]-1H-indene-2-carboxylate	515.83 g/mol	
IN-MP819		Degradate	lndenol[1 ,2-e][1 ,3,4]oxadlazine-1(2H)-carboxylic acid, 7-chloro-3,5-dlhydno-2-[[[4-(triftuoromethoxy)phenyl]amino]carbonyl]-, methyl ester	469.8 g/mol	Yes
IN-U8E24		Degradate of *S* Enantiomer	sodium (4aS)-7-chloro-2,5-dihydro-2-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3*H*)-carboxylate		
IN-UYG24		Degradate of *S* Enantiomer	Sodium(4aS)-2-(aminocarbonyl)-7-chloro-2,5-dihydroindeno [1,2-e] [l,3,4]oxadiazine-4a(3//)-carboxylate (1:1)	317.66 g/mole	

Chemical Common Name	Synonym in Submitted Studies	Comment	IUPAC Chemical Name	Molecular Weight	Residue of Concern for Aquatic Assessment?
Product Formulations (Based on Old Technical)					
DPX-MP062 150 EC	14.7% *S* 4.3% *R* mixture	14.7% *S* 4.3% *R* in formulation	(*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	527.84 g/mole	
DPX-MP062 30WG	29.3% *S* 10.3% *R* TEP; Formulation IN-30WG; DPX-KN128 30WG; Indoxacarb 30WG	29.3% *S*-enantiomer in formulation	(*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	527.84 g/mole	
Refined *R*-enantiomer (KN127) and Degradates of *R*-enantiomer					
DPX-KN127	IN-KN127	*R* Enantiomer	(*R*)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[l ,2-e]-[I ,3,4]oxadiazine-4a(3H)-carboxylate	527.84 g/mole	
DPX-KN124		Degradate of *R* Enantiomer	7-Chloro-2,5-dihydro-2[[[4-(trifiuoromethoxy)phenyl]amino]carbonyl]-, methyl ester, (4aR)-indeno[l ,2-e] [1,3,4]oxadiazine-4a(37/)-carboxylic acid	469.8 g/mole	

4.2 Degradates of Concern

As mentioned in the problem formulation (D408900), results of registrant-submitted studies indicate that degradate IN-JT333 is more acutely toxic to freshwater fish than parent indoxacarb and that degradate IN-MP819 is more acutely toxic to freshwater invertebrates than parent indoxacarb. Although degradate DPX-KN125 is highly toxic to rainbow trout with an LC_{50}=0.0098 mg a.i./L (MRID 49734502), its formation is minor (4.4%) in aerobic aquatic systems. Due to similar toxicities of DPX-KN125 and IN-JT333, the TEQ approach accounts for DPX-KN125 exposure when modeling IN-JT333. Therefore, indoxacarb and degradates IN-JT333 and IN-MP819 are considered stressors of concern in the assessment for aquatic animals (*i.e.*, fish and aquatic invertebrates). Due to this difference in degradate toxicities, the Toxic Equivalency Approach (TEQ; **Section 4.3**) was performed for aquatic exposure. Results inform the aquatic risk from the combined exposure to parent indoxacarb and degradates IN-JT333 and IN-MP819 (**Table 8**).

In previous indoxacarb assessments (D402424, D402425, D428813) that relied upon the TEQ approach, the Agency has relied upon environmental fate (EPI Suite4) estimates of model input parameters for IN-JT333 and IN-MP819. This assessment incorporates newly submitted registrant soil degradation and mobility studies on the degradates for these parameters (

Table 9).

Table 8. Empirical and estimated toxicity endpoints used for the calculation of Toxic Equivalency Ratios for adjusting estimated parent aquatic EECs.

Taxon	Endpoint	Parent Indoxacarb[a]		Degradate IN-JT333[a]		IN-JT333 TEQ (Ratio Indoxacarb:IN-JT333)	Degradate IN-MP819[a]		IN MP-819 TEQ (Ratio Indoxacarb:IN-MP819)
		mg/L	µmol/L	mg/L	µmol/L		mg/L	µmol/L	
Freshwater fish	Acute LC_{50}	0.29	0.55	0.024	0.05	10.7	>0.368	0.74	0.74
	Chronic NOEC	0.0675	0.13	0.00126	0.00	47.5	0.0849[b]	0.17	0.75
Estuarine/ marine fish	Acute LC_{50}	>0.37	0.70	0.014[b]	0.03	24.0	0.2095[b]	0.42	1.67
	Chronic NOEC	0.0169	0.03	0.0006[b]	0.00	24.0	0.0096[b]	0.02	1.67
Freshwater invertebrate	Acute EC_{50}	0.6	1.13	>0.029	0.06	18.35	0.064	0.13	8.84
	Chronic NOEC	0.00411	0.01	0.00020[b]	0.00	18.3	0.00044[b]	0.00	8.84
Estuarine/	Acute LC_{50}	0.0542	0.10	0.069	0.15	0.7	0.00578[b]	0.01	8.84

[4] https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

Taxon	Endpoint	Parent Indoxacarb[a]		Degradate IN-JT333[a]		IN-JT333 TEQ (Ratio Indoxacarb:IN-JT333)	Degradate IN-MP819[a]		IN MP-819 TEQ (Ratio Indoxacarb:IN-MP819)
		mg/L	µmol/L	mg/L	µmol/L		mg/L	µmol/L	
marine invertebrate	Chronic NOEC	0.0184	0.03	0.00347[b]	0.01	4.70	0.00196[b]	0.004	8.84
FW Benthic Invertebrates Bulk Sediment (mg/kg-sed)	Acute[c]	0.72							
	Chronic NOEC	0.00096	0.00	0.096	0.20	0.01	86.2	172.815	0.00
FW Benthic Invertebrates Pore Water	Acute[c]	1.4E-06							
	Chronic NOEC	0.00054	0.00	0.05432[b]	0.12	0.00	0.599	1.201	0.00

[a] See Ecological Effects Data section for description of the selected endpoints for the TEQ Ratios and parent toxicity values
[b] No empirical data available, estimated toxicity level based upon available data for other taxa (see Ecological Effects Data section)
[c] Acute toxicity of indoxacarb to benthic invertebrates was only evaluated on a chronic toxicity basis

Batch equilibrium and aerobic soil metabolism studies conducted on the degradates IN-JT333 and IN-MP819 indicate that the degradates are less mobile and less persistent than parent indoxacarb. An aerobic soil metabolism study (MRID 49577706) conducted with the degradate IN-JT333 for 122 days at 20ºC with five soils calculated half-lives ranging from 9.3 days to 66.5 days (90th percentile half-life = 41 days). Mineralization (CO2 evolution) ranged from 65% to 78% across all soils. The aerobic soil metabolism study (MRID 49912201) conducted with the degradate IN-MP819 for 120 days at 20ºC with three soils calculated half-lives ranging from 5.96 days to 37.6 days (90th percentile half-life = 40 days). Mineralization (CO2 evolution) ranged from 42% to 52% across all soils.

Batch equilibrium study (MRID 45795809) conducted on the degradate IN-JT333 indicates that the degradate is slightly mobile to hardly mobile in various soils according to FAO mobility classification (FAO, 2000). The adsorption Koc of IN-JT333 in four soils ranged from 8,200 to 25,000 mL/g-oc. A batch equilibrium study (MRID 49912202) conducted on the degradate IN-MP819 indicates that the degradate is slightly mobile to hardly mobile in loamy soils according to FAO mobility classification (FAO, 2000). The adsorption Koc of IN-MP819 in the three soils ranged from 6,560 to 13,541 mL/g-oc.

For indoxacarb's full degradation profile, see **Appendix C** for degradate information including structures and percent of formation. Unextracted residues were seen in aerobic and anaerobic soil systems and aerobic aquatic metabolism studies but not included in model half-life estimations since the half-life was conservative for the aerobic soil metabolism input (90th percentile half-life of 7 soils = 250 days) and unextracted residues were variable in the aerobic aquatic metabolism studies (90th percentile half-life of 10 systems = 41 days). It would be low value to add in unextracted residues into the aquatic exposure assessment given indoxacarb's toxicity profile to aquatic organisms. See **Appendix D** for proposed degradation pathways in aerobic soil and aerobic aquatic systems.

4.3 Toxic Equivalency Approach for Aquatic Exposure

A toxic equivalency (TEQ) approach is used to assess both parent indoxacarb and degradates IN-JT333 and IN-MP819. The EECs for parent only were compared to the endpoints to calculate RQs for aquatic plants. The following steps were taken to implement the TEQ approach and calculate acute and chronic RQs for each aquatic animal taxa:

a) Aquatic animal acute and chronic toxicity endpoints (mg/L) for parent indoxacarb and degradates IN-JT333 and IN-MP819 were converted to µmol/L using the molecular weight of each chemical[5] (

Table 9)

b) Ratios of the toxicity endpoint for parent indoxacarb (µmol/L) to the toxicity endpoint for each degradate (µmol/L) were calculated to yield Toxicity Equivalence Factors (TEFs).

c) Surface water EEC s of parent indoxacarb and degradates IN-JT333 and IN-MP819 were modeled separately in the Pesticide Water Calculator (PWC) using each chemical's physiochemical and fate properties (

Table 9**).** Model input parameters were chosen according to the current Input Parameter Guidance[6]. Daily time-series were retained from the output.

d) Surface water EEC time-series of IN-JT333 and IN-MP819 were adjusted based on the TEFs yielding surface water EEC time-series for the degradates expressed in toxic equivalents of parent.

e) The surface water EEC time-series for parent indoxacarb and surface water EEC time-series for degradates INJT333 and IN-MP819 expressed in toxic equivalents of parent were summed to yield a total surface water TEQ EEC time-series expressed in toxic equivalents of the parent.

f) Maximum peak, 21-day and 60-day concentrations were calculated for each year based on the TEQ EEC time-series, then the 1:10 year estimates were calculated (=TEQ EECs).

g) Toxic equivalent EECs were divided by the parent's toxicity endpoint to yield RQs.

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[5] Indoxacarb MW = 527.8 g/mol; IN-JT333 MW = 468.91 g/mol; IN-MP819 MW = 498.8

[6] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-selecting-input-parameters-modeling

An RQ calculated using the TEQ approach represents risk from combined exposure to parent indoxacarb and degradates IN-JT333 and IN-MP819.

Table 9. Input Parameters for Indoxacarb, IN-JT333 and IN-MP819

Input Parameter	Value	Comment	MRID
Indoxacarb			
Molecular Mass	527.8 g/mole	indoxacarb	product chemistry
Vapor Pressure (25 °C)	1.9 x 10^{-10} mm Hg		
Aqueous Solubility (20°C)	0.8 mg/L		
Organic Carbon Partition Coefficient (K_{OC}) (L/kg_{OC})	5125	Mean Koc value of parent values (2500, 3300, 5100, 9600)	45795809
Aerobic Soil Metabolism Half-life (days)	250 days	90^{th} percentile of 7 soils (3, 3, 6, 27, 10, 30, 693 days)	44477304 44477307 45850001 45166303
Aerobic Aquatic Metabolism Half-life (days)	41 days	90^{th} percentile of 10 systems (30.7, 39.8, 38.1, 21.3, 52.0, 58.0, 36.0, 42.0, 3.28, 5.37 days)	45793301 44477306 49577708
Anaerobic Aquatic Metabolism Half-life (days)	280 days	90^{th} percentile of 4 systems (192.5, 315.1, 147.0, 231.0 days)	44477305 45795804
Hydrolysis Half-life at pH 7 (days)	pH 7 = 36 days	90^{th} percentile of 3 values at pH 7 (38, 21.8, 17.4 days)	44477301 45795801 49577705
Aqueous Photolysis Half-life (days)	6.9 days	90^{th} percentile of 2 values (3.16, 5.0 days)	44477302 45795802
IN-JT333			
Molecular Mass	469.8 g/mole	IN-JT333	EpiSuite v 4.0 estimation
Vapor Pressure (25 °C)	1.3 x 10^{-11} mm Hg		
Aqueous Solubility (20°C)	0.05 mg/L		
Organic Carbon Partition Coefficient (K_{OC}) (L/kg_{OC})	17,300	Mean Koc value of 4 values (25,000, 12,000, 24,000, 8,200)	47595809

Input Parameter	Value	Comment	MRID
Aerobic Soil Metabolism Half-life (days)	41 days	90th percentile of 5 soils (11.3, 66.5, 14.4, 9.3, 20.3 days)	49577706
Aerobic Aquatic Metabolism Half-life (days)	180 days	IN-JT333	EpiSuite v 4.0 estimation
Anaerobic Aquatic Metabolism Half-life (days)	1621 days		
Hydrolysis Half-life at pH 7 (days)	stable		
Aqueous Photolysis Half-life (days)	stable		
IN-MP819			
Molecular Mass	469.8 g/mole	IN-MP819	EpiSuite v 4.0 estimation
Vapor Pressure (25 °C)	1.3×10^{-11} mm Hg		
Aqueous Solubility (20?C)	0.05 mg/L		
Organic Carbon Partition Coefficient (K_{OC}) (L/kg_{OC})	9658	Mean Koc value of 3 values (13,541, 8,873, 6,560)	49912202
Aerobic Soil Metabolism Half-life (days)	40 days	90th percentile of 3 soils (23.5, 5.96, 37.6 days)	49912201
Aerobic Aquatic Metabolism Half-life (days)	180 days	IN-MP819	EpiSuite v 4.0 estimation
Anaerobic Aquatic Metabolism Half-life (days)	1621 days		
Hydrolysis Half-life at pH 7 (days)	stable		
Aqueous Photolysis Half-life (days)	stable		

For the aquatic exposure modeling, application parameters were chosen based on the application method at the maximum application rate as indicated in the label instructions. Based on the labeled uses for indoxacarb, a variety of rates and locations simulated by EPA approved model PWC standard scenarios were run to estimate national use aquatic exposure estimates of indoxacarb**.** Not all indoxacarb uses were modeled but the scenarios were selected to be protective and capture differences in exposure potential due to differences in application rates, methods, frequency as well as differences in PWC model scenarios. A relative application date of 30 days from plant emergence was chosen since the application date was flexible depending on pest pressure. Spray drift fractions were based off the Agency's Spray Drift Guidance (USEPA, 2013b). For residental perimeter treatments, the non-standard (CA Residental and CA Impervious) scenarios were modeled separately then their time series were summed to estimate EECs. Residental and impervious coverage was based on a 1000 ft^2 footprint (see Table 11 footnotes for calculations). **Table 10** lists the modeled scenarios and input parameters describing the maximum patterns of Indoxacarb use on representative sites.

Table 10. Model Scenarios and Input Parameters Describing Maximum Patterns of Indoxacarb Use on Representative Use Sites

Use Site	PWC Scenario	Maximum single App. Rate[1] lbs a.i./A [kg a.i./ha]	Relative App. Date	App. per Year (seasons)	App. Interval (days)	App. Method	Application Efficiency	Spray Drift (%)
Agricultural Uses								
Alfalfa	CA Alfalfa IL Alfalfa MN Alfalfa NC Alfalfa TX Alfalfa	0.11 [0.124]	30	4 (1)	3	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Bean	MI Bean OR Snap Bean	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Beet	MN Sugarbeet	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Cucurbit	FL Cucurbit	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Grape Strawberry	CA Grape NY Grape FL Strawberry	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Leafy Greens/ Vegetables	CA Lettuce	0.065[0.073] 0.11 [0.124]	30	4 (1 and 4)	3	aerial ground	95% 99%	12.5% 6.2%
Pome Fruits	NC Apple OR Apple PA Apple	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%

Use Site	PWC Scenario	Maximum single App. Rate[1] lbs a.i./A [kg a.i./ha]	Relative App. Date	App. per Year (seasons)	App. Interval (days)	App. Method	Application Efficiency	Spray Drift (%)
Root and Tuber Vegetables	ID Potato ME Potato NC Sweet Potato	0.11 [0.124]	30	4 (1)	3	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Stone Fruit	MI Cherry GA Peach CA Fruit	0.11 [0.124]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Brassica Cole Crops	CA Cole Crop	0.065[0.073]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Mint	OR Mint	0.065[0.073]	30	4 (1)	3	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Fruiting Vegetables	FL Pepper CA Tomato FL Tomato PA Tomato	0.065[0.073]	30	4 (1)	3	aerial ground	95% 99%	12.5% 6.2%
Sweet Corn	FL Sweet Corn OR Sweet Corn	0.065[0.073]	30	4 (1)	3	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Cotton	CA Cotton MS Cotton NC Cotton	0.11 [0.124]	30	4 (1)	5	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Soybean	MS Soybean	0.11 [0.124]	30	4 (1)	5	aerial ground chemigation	95% 99% 100%	12.5% 6.2% 0%
Non-Agricultural Uses								
Residential Perimeter Treatments[2]	CA Residential CA Impervious	0.11 [0.124] 1.437 [1.61]	30	4 (1) 1 (1)	3	Granular Residential (10.2%)[3] Impervious (1.4%)[4]	100%	0%
Turf	FL Turf PA Turf	0.44 [0.494] 0.225 [0.253] 0.0375[0.042]	30	1 (1) 2 (1) 12 (1)	-- 7 7	ground	99%	6.2%

A = aerial application, G = Ground Application, C = chemigation

[1]= indoxacarb application rates. Degradate application rates adjusted for maximum degradate formation rate and molecular weight ratio adjustment. Example: Application rate for degradate IN-JT333 = parent application rate (lbs a.i./acre) x maximum formation rate in fate studies (0.282; MRID 44477305) x molecular weight ratio of IN-

JT333 to indoxacarb (0.89). Application rate for degradate IN-MP819 = parent application rate (lbs a.i./acre) x maximum formation rate in fate studies (0.213; MRID 49577708) x molecular weight ratio of IN-MP819 to indoxacarb (0.89)
[2]= Perimeter EECs = [residential EEC x residential fraction (0.102)] + [impervious EEC x impervious fraction (0.014)]
[3]= Residental coverage based on a 1000 ft^2 footprint (31.6 ft + 31.6 ft + 31.6 ft + 31.6 ft – 15 ft driveway x 10 foot perimeter treatment) on a per acre basis (1114 ft^2 /10890 ft^2)
[4]= Impervious coverage based on a 150 ft^2 footprint (15 ft driveway x 10-foot perimeter treatment) on a per acre basis (150ft^2 /10890 ft^2).

The PWC (PWC version 1.52; May 19, 2016[7]) model was used to generate EECs of indoxacarb that may occur in surface waters impacted by rainfall-runoff and spray drift, where non-target organisms can be exposed. Surface water exposure estimates for lettuce single- and 4-season applications are provided in **Table 11 and 12**. The PWC EECs for parent, and degradates were modeled on an individual basis and indicate significantly lower concentrations of the degradates for the peak, 21 and 60 day periods. Also provided in **Table 11** are the TEQ adjusted EECs for each individual taxon and duration. For some taxa, the TEQ EECs are approximately the same as those for parent only (e.g., EM Invert Acute), whereas for others the TEQ EEC is roughly double the parent EEC (e.g., FW Fish Chronic). These differences are attributable to the differential toxicity of the degradates (being much more toxic) to parent **(Table 12**). A full report of the TEQ EECs for all modeled uses and scenarios is provided in the risk description section for aquatic organisms**.**

Table 11. Estimated aquatic exposure concentrations for parent and degradate model results, and TEQ adjusted EECs for Lettuce following 4 aerial applications for one season.

PWC 90th Percentile Estimated Concentrations by Chemical (mg a.i./L)			
Chemical	**Peak**	**21-day**	**60-day**
Parent only EECs	0.00225	0.00146	0.00093
IN-JT333	0.00011	0.00004	0.00003
IN-MP819	0.00010	0.00004	0.00004
TEQ 90th Percentile Estimated Concentrations by Taxon and Duration (mg a.i./L)			
TEQ Category	**Peak**	**21-day**	**60-day**
FW Fish	0.0032	NA[a]	0.0024
EM Fish	0.0045	NA[a]	0.0017
FW Invert	0.0046	0.0023	NA[a]
EM Invert	0.0029	0.0019	NA[a]

[a] chronic EECs are 21- and 60-days for invertebrates and fish respectively

[7] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

Table 12. Estimated aquatic exposure concentrations for parent and degradate model results, and TEQ adjusted EECs for Lettuce following 4 aerial applications for four seasons.

PWC 90th Percentile Estimated Concentration by Chemical (mg a.i./L)			
Chemical	**Peak**	**21-day**	**60-day**
Parent only EECs	0.00709	0.00372	0.00283
IN-JT333	0.00019	0.00012	0.00011
IN-MP819	0.00017	0.00013	0.00012
TEQ 90th Percentile Estimated Concentration by Taxon and Exposure (mg a.i./L)			
TEQ Category	**Peak**	**21-day**	**60-day**
FW Fish	0.0089	NA[a]	0.0075
EM Fish	0.0110	NA[a]	0.0052
FW Invert	0.0111	0.0065	NA[a]
EM Invert	0.0085	0.0051	NA[a]

[a] Chronic EECs are 21- and 60-days for invertebrates and fish respectively

4.4 Monitoring Data

Indoxacarb monitoring data were not found in the California Department of Pesticide Regulation (CDPR) surface water database (Accessed on April 3, 2017, http://www.cdpr.ca.gov/docsb /emon/surfwtr/surfcont.htm) and in the NAWQA water quality portal (WQP) (Accessed on April 3, 2017, http://waterqualitydata.us/), which integrates public available water quality data from the USGS National Water Information System (NWIS), the EPA STOrage and RETrieval (STORET) Data Warehouse, and the USDA ARS Sustaining The Earth's Watersheds Agricultural Research Database System (STEWARDS).

4.5 Terrestrial Organism Exposures

4.5.1 Birds and Mammals

For birds and mammals, the terrestrial organism exposures were modeled using a subset of the application rates for agricultural foliar sprays, and non-agricultural uses including fire ant granules and perimeter sprays. Crack and crevice/spot treatment uses (See Appendix B) were not considered in this assessment due to reduced exposure potential compared to the general surface and perimeter sprays. Pet spot-on treatments for fleas also are not considered in this assessment because of the minimal potential environmental exposures.

For agricultural and non-agricultural uses, the minimum and maximum application rates and their respective uses were modeled in order to create a bracket of possible RQs for the range of application rates and intervals registered for indoxacarb. For agricultural uses, the minimum application of indoxacarb was a series of 4 applications (i.e., 0.0625 lbs a.i./acre, 3-day application interval, 4 maximum applications), to investigate risk to birds and mammals at the most conservative scenario. A single application was modeled for characterization purposes only. For non-agricultural uses, again the application rates were bracketed and modeled for the minimum and maximum application rates for perimeter sprays, turf, and ornamental lawns (**See Use Characterization Section**).

The granular form of indoxacarb (represented by Adivon Fire Ant Granule) was modeled and characterized separately using the LD_{50}/ft^2 (T-REX (v1.5.2)[8] approach.

All scenarios consider a single seasonal application; however, the product can be applied for multiple seasons in a year (similar to the aquatic assessment) for certain crops including leafy greens, beans and root and tuber vegetables (**see Use Characterization Section**). The on-field terrestrial assessment considered only one seasonal application since crops will be removed from the field post-harvest and application, thus minimizing the cumulative burden of multiple season expsoures. However, the spray drift footprint modeling considered off-field risks, in which birds and mammals are exposed to the multiple applications of indoxacarb.

Food item based EEC Method

There are no data available to modify the default foliar half-life estimate of 35-days. The EECs on food items may be compared directly with sub-acute dietary toxicity data or converted to an ingested whole-body dose (single oral dose). Exposure from foliar application (residues on food) is estimated for birds and mammals in **Table 13-Table 14.**

Table 13. Estimated environmental concentrations on mammalian and avian food items for indoxacarb agricultural uses

Food Items	Dietary-based EECs mg/kg-diet
Foliar Spray Application at 0.0.0625 lb a.i./acre; a single application	
Short Grass	15.00
Tall Grass	6.88
Broadleaf/forage plants and small insects	8.44
Fruits/pods/seeds	0.94
Arthropods	5.88
Foliar Spray Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)	
Short Grass	55.01
Tall Grass	25.21

[8] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

Broadleaf/forage plants and small insects	30.94
Fruits/pods/seeds	3.44
Arthropods	21.54
Foliar Spray Application at 0.1125 lb a.i./acre, 5- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for cotton and soybeans	
Short Grass	93.66
Tall Grass	42.93
Broadleaf/forage plants and small insects	52.69
Fruits/pods/seeds	5.85
Arthropods	36.69
Foliar Spray Application at 0.1125 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for to alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens	
Short Grass	99.01
Tall Grass	45.38
Broadleaf/forage plants and small insects	55.69
Fruits/pods/seeds	6.19
Arthropods	38.78

Table 14. Estimated environmental concentrations on mammalian and avian food items for indoxacarb non-agricultural uses

Food Items	Dietary-based EECs mg/kg-diet
Foliar Spray Application at 0.0375 lb a.i./acre, 7-day application interval and 12 applications per year at a maximum seasonal rate of 0.45 lbs a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf	
Short Grass	56.35
Tall Grass	25.83
Broadleaf/forage plants and small insects	31.70
Fruits/pods/seeds	3.52
Arthropods	22.07
Foliar Spray Application at 0.225 lb a.i./acre, 7-day application interval and 2 maximum applications per year at a maximum seasonal rate of 0.45 lb a.i./acre for ornamental lawns and turf	
Short Grass	101.01
Tall Grass	46.30
Broadleaf/forage plants and small insects	56.82
Fruits/pods/seeds	6.31
Arthropods	39.56
Foliar Spray Application at 1.437 lb a.i./acre, 7-day application interval and 12 maximum applications for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites	
Short Grass	2159.43
Tall Grass	989.74
Broadleaf/forage plants and small insects	1214.68
Fruits/pods/seeds	134.96
Arthropods	845.78

EEC Equivalent Dose Based Method

The residues or EECs on food items may be compared directly with subacute dietary toxicity data or converted to an ingested whole-body dose (single oral dose, as the latter is the case for small mammals and birds). Single-oral dose estimates represent, for many pesticides, an exposure scenario where absorption of the pesticide is maximized over a single ingestion event. Subacute dietary estimates provide for possible effects of the dietary matrix and more extended time of gut exposure on pesticide absorption across the gut. However, dietary exposure endpoints are limited in their utility because the current food ingestion estimates are uncertain and may not be directly comparable from laboratory conditions to field conditions. The EEC is converted to an oral dose by multiplying the EEC by the percentage of body weight consumed as estimated through allometric relationships. These consumption-weighted EECs (i.e. EEC equivalent dose) are determined for each food source and body size for birds (20, 100, and 1000 g) and mammals (15, 35, and 1000 g) **(Table 15-Table 18**). The output from T-REX is included in **Appendix E.**

Table 15. Avian EEC equivalent dose adjusted for Avian EEC Equivalent Dose Adjusted for Body Weight for Indoxacarb agricultural uses

EEC Equivalent Dose (mg/kg-bodyweight)	**Avian Classes and Body Weights**		
	Small (20g)	**Mid (100g)**	**Large (1000g)**
Percent Body Weight Consumed	114%	65%	29%
Foliar Spray Applications at 0.0.0625 lb a.i./acre, 3- day application interval, and a single application			
Short Grass	17.08	9.74	4.36
Tall Grass	7.83	4.46	2.00
Broadleaf plants/small insects	9.61	5.48	2.45
Fruits/pods	1.07	0.61	0.27
Arthropods	6.69	3.82	1.71
Seeds	0.24	0.14	0.06
Foliar Spray Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)			
Short Grass	59.26	33.79	15.13
Tall Grass	27.16	15.49	6.93
Broadleaf plants/small insects	33.34	19.01	8.51
Fruits/pods	3.70	2.11	0.95
Arthropods	23.21	13.24	5.93
Seeds	0.82	0.47	0.21
Foliar Spray Application at 0.1125 lb a.i./acre, 5- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for cotton and soybeans			
Short Grass	106.67	60.83	27.23
Tall Grass	48.89	27.88	12.48
Broadleaf plants/small insects	60.00	34.22	15.32
Fruits/pods	6.67	3.80	1.70
Arthropods	41.78	23.83	10.67

EEC Equivalent Dose (mg/kg-bodyweight)	Avian Classes and Body Weights		
	Small (20g)	Mid (100g)	Large (1000g)
Seeds	1.48	0.84	0.38
Foliar Spray Application at 0.1125 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for to alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens			
Short Grass	112.76	64.30	28.79
Tall Grass	51.68	29.47	13.19
Broadleaf plants/small insects	63.43	36.17	16.19
Fruits/pods	7.05	4.02	1.80
Arthropods	44.17	25.18	11.28
Seeds	1.57	0.89	0.40

Table 16. Avian EEC Equivalent Dose Adjusted body weight for indoxacarb non-agricultural uses.

EEC Equivalent Dose (mg/kg-bodyweight)	Avian Classes and Body Weights		
	Small (20g)	Mid (100g)	Large (1000g)
Percent Body Weight Consumed	114%	65%	29%
Foliar Spray Application at 0.0375 lb a.i./acre, 7-day application interval and 12 applications per year at a maximum seasonal rate of 0.45 lbs a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf			
Short Grass	64.18	36.00	16.39
Tall Grass	29.42	16.77	7.51
Broadleaf plants/small insects	36.10	20.59	9.22
Fruits/pods	4.01	2.29	1.02
Arthropods	25.14	14.33	6.42
Seeds	0.89	0.51	0.23
Foliar Spray Application at 0.225 lb a.i./acre, 7-day application interval and 2 maximum applications per year at a maximum seasonal rate 0f 0.45 lb a.i./acre for ornamental lawns and turf			
Short Grass	115.04	65.60	29.37
Tall Grass	52.73	30.07	13.46
Broadleaf plants/small insects	64.71	36.9	16.52
Fruits/pods	7.19	4.10	1.84
Arthropods	45.06	25.59	11.50
Seeds	1.60	0.91	0.41
Foliar Spray Application at 1.437 lb a.i./acre, 7-day application interval and 12 maximum applications for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites			
Short Grass	2459.38	1402.44	627.89
Tall Grass	1127.22	642.79	287.78
Broadleaf plants/small insects	1383.40	788.87	353.19
Fruits/pods	153.71	97.65	39.24

EEC Equivalent Dose (mg/kg-bodyweight)	Avian Classes and Body Weights		
	Small (20g)	Mid (100g)	Large (1000g)
Arthropods	963.26	549.29	245.92
Seeds	34.16	19.48	8.72

Table 17. Mammalian EEC Equivalent Dose Adjusted for Body Weight for Indoxacarb for agricultural uses.

EEC Equivalent Dose (mg/kg-bodyweight)	Mammalian Classes and Body Weights		
	Small (15)	Mid (35g)	Large (1000g)
Percent Body Weight Consumed	95%	66%	15%
Foliar Spray Applications at 0.0625 lb a.i./acre, 3- day application interval, and a single application			
Short Grass	14.30	9.88	2.29
Tall Grass	6.55	4.53	1.05
Broadleaf plants/small insects	8.04	5.56	1.29
Fruits/pods	0.89	0.62	0.14
Arthropods	5.60	3.87	0.90
Seeds	0.20	0.14	0.03
Foliar Spray Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)			
Short Grass	52.44	36.25	8.40
Tall Grass	24.04	16.61	3.85
Broadleaf plants/small insects	29.50	20.39	4.73
Fruits/pods	3.28	2.27	0.53
Arthropods	20.54	14.20	3.29
Seeds	0.73	0.50	0.12
Foliar Spray Application at 0.1125 lb a.i./acre, 5- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for cotton and soybeans			
Short Grass	89.30	61.72	14.31
Tall Grass	40.93	28.29	6.56
Broadleaf plants/small insects	50.23	34.72	8.05
Fruits/pods	5.58	3.86	0.89
Arthropods	34.98	24.17	5.60
Seeds	1.24	0.86	0.20
Foliar Spray Application at 0.1125 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for to alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens			
Short Grass	94.40	35.24	15.13
Tall Grass	43.27	29.90	6.93
Broadleaf plants/small insects	5310	36.70	8.51
Fruits/pods	5.90	4.08	0.95
Arthropods	36.97	25.55	5.92
Seeds	1.31	0.91	0.21

Table 18. Mammalian EEC Equivalent Dose Adjusted body weight for indoxacarb non-agricultural uses.

EEC Equivalent Dose (mg/kg-bodyweight)	**Mammalian Classes and Body Weights**		
	Small (15g)	**Mid (35g)**	**Large (1000g)**
Percent Body Weight Consumed	114%	65%	29%
Foliar spray Application at 0.0375 lb a.i./acre, 7-day application interval and 12 applications per year at a maximum seasonal rate of 0.45 lbs a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf			
Short Grass	53.73	37.13	8.61
Tall Grass	24.63	17.02	3.95
Broadleaf plants/small insects	30.22	20.89	4.84
Fruits/pods	3.36	2.32	0.54
Arthropods	21.04	15.54	3.37
Seeds	0.75	0.52	0.12
Foliar spray broadcast 0.225 lb a.i./acre, 7-day application interval and 2 maximum applications per year at a maximum seasonal rate 0f 0.45 lb a.i./acre for ornamental lawns and turf.			
Short Grass	96.31	66.56	15.43
Tall Grass	44.14	30.51	7.07
Broadleaf plants/small insects	54.17	37.44	8.68
Fruits/pods	6.02	4.16	0.96
Arthropods	37.72	26.07	6.04
Seeds	1.34	0.92	0.21
Foliar spray broadcast at 1.437 lb a.i./acre, 7-day application interval and 12 maximum applications for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites			
Short Grass	2085.85	1422.94	329.91
Tall Grass	943.64	652.18	151.21
Broadleaf plants/small insects	1158.11	800.41	184.58
Fruits/pods	128.68	88.93	20.62
Arthropods	806.38	557.32	129.22
Seeds	28.60	19.76	4.58

Granular EECs

For the indoxacarb fire ant granule, risk was assessed based on the toxicity of the TGAI since there were no effects data submitted for the Adivon fire ant product. Indoxacarb is applied to the soil surface as a granule (as indicated on the label Reg. #100-1483) and it is assumed that the entire granule is consumed by the bird or mammal. The LD_{50}/ft^2 approach was used to model the two granular scenarios for application of Adivon Insect Granule. For the 0.11 lb a.i./acre granular application rate the EEC was 1.15 mg a.i./ft^2 and for the 0.44 mg a.i./acre application rate the EEC was 4.58 mg a.i./ft^2.

KABAM

The consumption of aquatic organisms that have accumulated indoxacarb may serve as an additional exposure route for higher trophic level organisms. Risk through consumption of contaminated food was evaluated and modeled using the KABAM model (v. 1.0). EEC pore water and water column values were selected for both indoxacarb parent and for the total toxic residues of the degradates of indoxacarb, reflecting the time closest to steady state. The scenarios modeled the highest agricultural EECs across applications for both single seasons and multiple seasons. Inputs to the model are summarized below (**Table 19-21**). The model assumes that the metabolic rate elimination constant in fish (k_m=0). However, for indoxacarb, the major degradate of concern is IN-JT333, which is highly toxic to mammals. This is supported by the bioconcentration and metabolism study in fish, indicating that fish exposed to the indoxacarb parent in water metabolize the parent into JT-333, MP7819 (MRID 44477319).

Table 19. Chemical characteristics of indoxacarb parent for input into KABAM

Characteristic	Value	Comments/Guidance
Pesticide Name	Indoxacarb (Parent)	
Log K_{OW}	4.65	Enter value from acceptable or supplemental study submitted by registrant or available in scientific literature.
K_{OW}	44668	No input necessary. This value is calculated automatically from the Log K_{OW} value entered above.
K_{OC} (L/kg OC)	5125	Input value used in PRZM/EXAMS to derive EECs. Follow input parameter guidance for deriving this parameter value (USEPA 2002).
Time to steady state (T_S; days)	14	No input necessary. This value is calculated automatically from the Log K_{OW} value entered above.
Indoxacarb Parent Most Sensitive Effects Endpoints		
Avian	LD_{50} (mg/kg-bw)	98 (northern bobwhite quail)
	LC_{50} (mg/kg-diet)	808 (northern bobwhite quail)
	NOAEC (mg/kg-diet)	114 (northern bobwhite quail)
Mammalian	LD_{50} (mg/kg-bw)	179 (laboratory rat)
	LC_{50} (mg/kg-diet)	N/A
	Chronic Endpoint	40 (laboratory rat)

Table 20. Conservative chemical characteristics for input into KABAM under the Total Toxic Residue (TTR) approach

Characteristic	Value	Comments/Guidance
Pesticide Name	Indoxacarb (TTR)	
Log K_{OW}	5	Enter value from acceptable or supplemental study submitted by registrant or available in scientific literature.
K_{OW}	100000	No input necessary. This value is calculated automatically from the Log K_{OW} value entered above.
K_{OC} (L/kg OC)	17300	Input value used in PRZM/EXAMS to derive EECs. Follow input parameter guidance for deriving this parameter value (USEPA 2002).
Time to steady state (T_S; days)	14	No input necessary. This value is calculated automatically from the Log K_{OW} value entered above.
Mammalian and avian toxicity data for indoxacarb adjusted by molecular weight		
Avian	LD_{50} (mg/kg-bw)	110.1 (northern bobwhite quail)
	LC_{50} (mg/kg-diet)	907.38 (northern bobwhite quail)
	NOAEC (mg/kg-diet)	128 (northern bobwhite quail)
Mammalian	LD_{50} (mg/kg-bw)	39 (laboratory rat)
	LC_{50} (mg/kg-diet)	N/A
	Chronic Endpoint	44.92 (laboratory rat)

Table 21. EEC Inputs used in KABAM Modeling

Crop	Application Rate, Method, and Interval	PWC Scenario	14-day Pore Water Concentration (µg/L)	14-day Water Column Concentration (µg/L)
Indoxacarb				
Cotton	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0004	1.17
		MS Cotton	0.001	2.25
		NC Cotton	0.0012	2.09
	0.11 lbs a.i./A x 4 Ground 5-day interval	CA Cotton	0.0004	0.65
		MS Cotton	0.0009	2.19
		NC Cotton	0.0011	1.86

Crop	Application Rate, Method, and Interval	PWC Scenario	14-day Pore Water Concentration (µg/L)	14-day Water Column Concentration (µg/L)
Soybean	0.11 lbs a.i./A x 4 Aerial 5-day interval	MS Soybean	0.0008	1.77
	0.11 lbs a.i./A x 4 Ground 5-day interval	MS Soybean	0.0006	1.35
Leafy Vegetables	0.11 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0023	4.36
	0.065 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0014	2.56
	0.11 lbs a.i./A x 4 Aerial 3-day interval 1 season	CA Lettuce	0.0007	1.65
Non-Agricultural Turf				
Turf	0.44 lbs a.i./A x 1 Ground	PA Turf	0.0003	0.81
		FL Turf	0.0002	0.75
Estimated TTR[1]				
Leafy Vegetables	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0005	1.25
	0.11 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0024	4.41

[1] The estimated TTR is a summation of the individual PWC concentration time series (not adjusted for toxicity ratios) as modeled for the TEQ process, followed by the 1 in 10-year estimation.

Drinking Water and Inhalation

The maximum application rates and worst case inhalation and drinking water exposure scenarios were screened using the STIR (Screening Tool for Inhalation Risk) and SIP (Screening Imbibition Program) and models[6]. A representative model input and output and results are presented in the Problem Formulation (USEPA 2013a).

[6] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#sip

4.5.2 Terrestrial Invertebrates

This draft risk assessment evaluates the risk of the registered uses of indoxacarb to bees. Consistent with the EPA 2014 *Guidance for Assessing Pesticide Risks to Bees* (USEPA/PMRA/CDPR, 2014), risks are quantified for the honey bee, *Apis mellifera*. Bees may be exposed to indoxacarb through direct contact, residues in pollen and nectar, contaminated surface water, plant guttation fluids, honey dew, soil (for ground-nesting bees), and leaves. However, there is high uncertainty regarding the importance of some of these exposure routes, and the Agency lacks information to understand the relative importance of these other routes of exposure and/or to quantify risks from these other routes. The primary routes of exposure being assessed quantitatively in this assessment are the contact and oral routes. These are considered the dominant exposure routes for indoxacarb. Measures of contact exposure include the estimated contact dose on a per bee basis (*e.g.,* µg a.i./bee). Oral exposure is also determined on a mass active ingredient (a.i.) per bee basis and considers ingestion of contaminated pollen and nectar. Bees may also be exposed to pesticides through other routes of exposure such as through plant guttation fluid, surface water, soil (for ground nesting bees) and drift of abraded seed coat dust, but those are considered uncertain and do not all apply to indoxacarb uses.

The bee risk assessment process is a tiered approach that begins with model-generated (based on consumption rates of pollen and nectar and application rate) or default estimates of exposure and laboratory toxicity data at the individual level (Tier I). These estimates are also based on the bee's life stage (*i.e.,* adult vs larvae) and the method of application (*i.e.,* foliar, soil, or seed treatment applications). In Tier I, pesticide exposures are estimated based on honey bee castes with known high-end consumption rates. For larvae, food consumption rates are based on 5-day old larvae, which consume the most food compared to other days of this life stage. For adults, the method relies upon nectar foraging bees, which consume the greatest amount of nectar of all castes while nurse bees consume the greatest amount of pollen. It is assumed that these high-end exposures will be comparable to the consumption rates of adult drones (males) and will be protective for adult queens as well. Although the queen consumes more food than adult workers or drones, the queen consumes "processed" food (*i.e*., royal jelly produced by the hypopharyngeal glands of nurse bees) that is assumed, based on currently available data, to contain orders of magnitude less pesticide than that consumed by adult workers.

Pollen and Nectar Route of Exposure

Honey bees are exposed to both pollen and nectar, which serve as the protein and carbohydrate sources in the diet, respectively. The risk assessment for individual bees assumes that the pesticide concentration in the two food sources is equal and that there is no influence of the food matrix on toxicity at the individual level. No information was identified that enabled these assumptions to be directly evaluated at the individual organism level. Nectar is the major food source for foraging honey bees as well as nurse bees (young, in-hive females). Therefore, pesticide residues in nectar likely account for most of the exposures to bees, and may represent most of the potential risk concerns for adult bees. However, if residues in pollen are of concern, exposures to nurse bees, which consume more pollen than any other adult honey bees, should be considered. This is the case especially when pesticide concentrations in pollen are much greater than in nectar, or for crops that mainly provide pollen to bees and would be assessed on a case-by-case basis.

Foliar Sprays

Many factors determine the exposure of bees to a pesticide. These include methods and timing of application, application rate, attractiveness of the crop to bees, and agronomic practices such as harvesting crops prior to bloom. Foliar application of pesticides, expected to result in exposure of bees by two dominant routes: 1) direct contact with the bee via interception of pesticide spray droplets and newly-sprayed vegetation, and 2) oral ingestion through contaminated pollen and nectar. With foliar sprays, these routes of exposure may occur on the treated field, or in the case of spray drift, adjacent to the treated field. With honey bees, nectar and pollen foragers are expected to receive high exposure via their frequent interaction with blooming crops. Dominant exposure routes of in-hive bees (*e.g.*, nurse, queen, drone bees) include ingestion and processing of pollen and nectar and exposure through production. Stored honey is expected to be an important exposure route for over wintering bees. Processed bee bread, brood food, and royal jelly are major routes of exposure for developing larvae and the queen, although limited evidence suggests pesticide levels in royal jelly are orders of magnitude below those found in pollen and nectar (USEPA, 2012).

The Tier I risk estimation model for honey bees (Bee-Rex; v.1.0[9]) allows calculation of exposure and resulting RQs for all types of bee castes. This method is intended to account for the major routes of pesticide exposure that are relevant to bees (*i.e*., through diet and contact). Exposure routes for bees differ based on application type. In the model, bees foraging in a field treated with a pesticide through foliar spray could potentially be exposed to the pesticide through direct spray as well through consuming contaminated food. For honey bees foraging in fields treated with a pesticide through direct application to soil (*e.g.*, drip irrigation), through seed treatments, or through tree injection, direct spray onto bees is not expected. For these application methods, pesticide exposure through consumption of residues in nectar and pollen are expected to be the dominant routes. **Table 22** below (extracted from *Guidance for Assessing Pesticide Risks to Bees*, USEPA/PMRA/CDPR, 2014) summarizes the exposure estimates for contact and dietary exposures for adult and larvae resulting from foliar, soil, seed treatment and tree injection application of pesticides.

[6] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

Table 22. Summary of Contact and Dietary Exposure Estimates for Foliar Applications, Soil Treatment, Seed Treatments, and Tree Trunk Injections of Pesticides for Tier I Risk Assessments

Measurement Endpoint	Exposure Route	Exposure Estimate*
Foliar Applications		
Individual Survival (adults)	Contact	$AR_{English}$*(2.7 μg a.i./bee) AR_{Metric}*(2.4 μg a.i./bee)
Individual Survival (adults)	Diet	$AR_{English}$ *(110 μg a.i /g)*(0.292 g/day) AR_{Metric} *(98 μg a.i /g)*(0.292 g/day)
Brood size and success	Diet	$AR_{English}$ *(110 μg a.i /g)*(0.124 g/day) AR_{Metric} *(98 μg a.i /g)*(0.124 g/day)
Soil Treatments		
Individual Survival (adults)	Diet	(Briggs EEC)*(0.292 g/day)
Brood size and success	Diet	(Briggs EEC)*(0.124 g/day)
Seed Treatments		
Individual Survival (adults)	Diet	(1 μg a.i /g)*(0.292 g/day)
Brood size and success	Diet	(1 μg a.i /g)*(0.124 g/day)
Tree Trunk Applications[++]		
Individual Survival (adults)	Diet	(μg a.i. applied to tree/g of foliage)*(0.292 g/day)
Brood size and success	Diet	(μg a.i. applied to tree/g of foliage)*(0.124 g/day)

$AR_{English}$ = application rate in lbs a.i./A; AR_{Metric} = application rate in kg a.i./ha
*Based on food consumption rates for larvae (0.124 g/day) and adult (0.292 g/day) worker bees and concentration in pollen and nectar.
++Note that concentration estimates for tree applications are specific to the type and age of the crop to which the chemical is applied.

The consumption of nectar and pollen vary depending on the bee's life stage and caste within the hive. The consumption rates tabulated below inform the exposure estimates and resultant RQs in the default Tier I and refined Tier I analyses that are presented in **Table 23** (USEPA/PMRA/CDPR, 2014). Additional detail of the derivation of these consumption rates can be found in the White Paper (USEPA, 2012).

Table 23. Summary of Estimated Food Consumption Rates for Bees

Life Stage	Caste (task in hive[a])	Average age (in days)[a]	Daily consumption rate (mg/day)			
			Jelly	Nectar[b]	Pollen	Total
Larval	Worker	1	1.9	0	0	1.9
		2	9.4	0	0	9.4
		3	19	0	0	19
		4	0	60[c]	1.8[d]	62
		5	0	120[c]	3.6[d]	124
	Drone	6+	0	130	3.6	134
	Queen	1	1.9	0	0	1.9
		2	9.4	0	0	9.4
		3	23	0	0	23
		4+	141	0	0	141
Adult	Worker (cell cleaning and capping)	0-10	0	60[f]	1.3 - 12[g,h]	61 - 72
	Worker (brood and queen tending, nurse bees)	6-17	0	113 - 167[f]	1.3 - 12[g,h]	114 - 179
	Worker (comb building, cleaning and food handling)	11-18	0	60[f]	1.7[g]	62
	Worker (foraging for pollen)	>18	0	35 - 52[f]	0.041[g]	35 - 52
	Worker (foraging for nectar)	>18	0	292 (median)[c]	0.041[g]	292
	Worker (maintenance of hive in winter)	0-90	0	29[f]	2[g]	31
	Drone	>10	0	133 - 337[c]	0.0002[c]	133 - 337
	Queen (laying 1500 eggs/day)	Entire lifestage	525	0	0	525

[a] Winston (1987)
[b] Consumption of honey is converted to nectar-equivalents using sugar contents of honey and nectar.
[c] Calculated as described in this paper.
[d] Simpson (1955) and Babendreier *et al.* (2004)
[e] Pollen consumption rates for drone larvae are unknown. Pollen consumption rates for worker larvae are used as a surrogate.
[f] Based on sugar consumption rates of Rortais *et al.* (2005). Assumes that average sugar content of nectar is 30%.
[g] Crailsheim *et al.* (1992, 1993)
[h] Pain and Maugenet 1966

Contact and dietary (pollen and nectar) EECs were estimated using BeeRex v1.0 model. EECs were modeled at an application rates for both agriculture and non-agricultural uses. EECs are presented in **Table 24-25.** <u>The selected modeled application rates bracket the non-agricultural and agricultural application rates and are considered to provide an estimation of exposure for all labeled uses.</u>

Table 24. EECs for contact and dietary exposure routes for honeybees for agricultural uses

Use	**EECs[1]**
Liquid Ground Broadcast Application at 0.06525 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)	
Foliar Spray	7.178 mg a.i./kg (Contact) 0.00718 µg a.i./mg (Dietary)
Soil Application	4.62x10^{-5} µg a.i./mg (Dietary)
Liquid Ground Broadcast Application at 0.1125 lb a.i./acre for cotton and soybeans, alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens	
Foliar spray	12.375 mg a.i./kg (Contact) 0.0123 µg a.i./mg (Dietary)
Soil Application	7.97 x 10^{-5} µg a.i./mg (Dietary)

[1] Soil application was calculated with a log k_{ow} = 4.65 and a k_{oc} = 5125

Table 25. EECs for contact and dietary exposure routes for honeybees for non-agricultural uses.

Use	**EECs[1]**
Ground spray application at 0.0375 lb a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf	
Foliar Spray	4.125 mg a.i./kg (Contact) 0.004 µg a.i./mg (Dietary)
Soil Application	2.65 x 10^{-5} µg a.i./mg (Dietary)
Ground spray broadcast 0.225 lb a.i./acre for ornamental lawns and turf	
Foliar spray	24.75 mg a.i./kg (Contact) 0.02475 µg a.i./mg (Dietary)
Soil Application	0.000159 µg a.i./mg (Dietary)
Ground spray broadcast at 1.437 lb a.i./acre for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites	
Foliar spray	158.07 mg a.i./kg (Contact) 0.15807 µg a.i./mg (Dietary)
Soil Application	0.00102 µg a.i./mg (Dietary)

[1] Soil application was calculated with a log k_{ow} = 4.65 and a k_{oc} = 5125

Potential for Exposure to Bees

The first step in the tiered bee risk assessment process is assessing the potential for exposure to adult and larval honey bees for a given use pattern. The determination for potential on-field exposure is based on whether the crop is attractive to bees and the agricultural practices, such as whether the crop is harvested prior to or after the bloom period (**Table 26**). The potential for on-field exposure is presumed for crops harvested after bloom and which are attractive to visiting honey bees, while off-field exposure is pertinent only for foliar uses, whether the crop is attractive to bees or not, as a result of spray drift.

Table 26. Bee Attractiveness for registered indoxacarb foliar and soil uses (as indicated by USDA, 2015)[1]

Crop Group Number	Honey Bee Attractive	Bumble Bee Attractive?	Solitary Bee Attractive?	Notes	Application Type	Potential for on-field Exposure? [a]	Potential for off-field Exposure? [b]
Crop Group 1 Root and Tuber Vegetables: -Subgroups 1A Beets -1C: Potato	Yes (Pollen and Nectar)*	Yes	Yes	Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom	Foliar	Yes	Yes
Crop Group 6 Legume Vegetables (succulent or dried) 6C (Dry succulent, except soybeans) 6A Edible-podded legume vegetables subgroup (soybeans)	Yes (Pollen and Nectar)	Yes	Yes		Foliar	Yes	Yes
Crop Group 13-07 Berry and Small Fruit -Subgroups 13-07D small vine climbing subgroup (except fuzzy kiwi) -13-07A Cranberry subgroup -13-07F Grapes	Yes (Pollen and Nectar)	Yes Grapes do not attract bumblebees	Yes Grapes do not attract solitary bees	**(Grapes are wind pollinated and do not require pollination via honeybees)**	Foliar	Yes	Yes
Peanuts	Yes (pollen and nectar)	Yes	Yes		Foliar	Yes	Yes
-Crop Group 4. Leafy Vegetables (Except Brassica Vegetables):	Yes (Pollen and nectar)	Yes	Yes	Bees important for seed production, typically harvested prior to bloom.	Foliar	No – however exposure may occur under seed production	Yes
-Crop Group 5 (Brassica Leafy Vegetables): Crop Sub-groups 5A & 5-B.	Yes (Pollen and nectar)	Yes	Yes	Bees important for seed production, typically harvested prior to bloom.	Foliar	No - however exposure may occur under seed production	Yes
Crop Group 9 (Cucurbit Vegetables)	Yes (Pollen and nectar)	Yes	Yes		Foliar	Yes	Yes

Crop Group Number	Honey Bee Attractive	Bumble Bee Attractive?	Solitary Bee Attractive?	Notes	Application Type	Potential for on-field Exposure? [a]	Potential for off-field Exposure? [b]
Crop Group 11 (Pome Fruits)	Yes (Pollen and Nectar)	Yes	Yes		Foliar	Y	Yes
Crop Group 12 Stone Fruits Subgroup 12-12-B	Y (Pollen and Nectar)	Yes	Yes		Foliar	Yes	Yes
Group 18 Nongrass animal feeds (forage, fodder, straw and hay) -Subgroup A (alfalfa)	Yes (Pollen and Nectar)	Yes	Yes		Foliar	Yes	Yes
Mint/peppermint/ spearmint	Yes	Yes	Yes		Foliar	Yes	Yes
Group 20 Oilseed group Subgroup 20C-Cotton	Yes (Nectar only)	Yes	Yes		Foliar	Yes	Yes
Group 15 Cereal Grains (sweet corn)	Yes (Pollen only)	NA	Yes	Wind pollinated, but can be visited during pollen shedding.	Foliar	Yes	Yes
Group 18-10 Fruiting vegetable Subgroup 18C (Okra)	Yes (Pollen and Nectar)	Y	Y		Foliar	Yes	Yes

a. The Potential for Off-Field Exposure Is Indicated from All Foliar Uses.
b. Spray drift is the main concern for off-field exposures
http://www.ree.usda.gov/ree/news/Attractiveness_of_Agriculture_crops_to_pollinating_bees_Report-FINAL.pdf

4.5.3 Terrestrial and Semi-Aquatic Plant Exposures

Indoxacarb exposure concentration to non-target plants was estimated using TerrPlant v 1.2[6] using the maximum agricultural application rates. EECs were modeled for a use scenario with an application rate of 0.0625 lb a.i./acre and 0.11 lb a.i./acre for aerial and ground liquid and granular ground applications. EECs are presented in **Table 27-Table 29).**

Table 27. Terrestrial Plant EECs for Indoxacarb (lbs a.i./A) for agricultural uses

EEC lb a.i./A					
Spray Drift		**Total for Dry Areas**		**Total for Semi-Aquatic Areas**	
Aerial Liquid	**Ground Liquid**	**Aerial Liquid**	**Ground Liquid**	**Aerial Liquid**	**Ground Liquid**
Foliar Spray Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)					
0.003125	0.000625	0.00125	0.00375	0.006875	0.009375
Foliar Spray Application at 0.1125 lb a.i./acre for cotton and soybeans, alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens					
0.0055	0.0011	0.0066	0.0022	0.0165	0.0121

Table 28. Terrestrial Plant EECs for Indoxacarb (lbs a.i./A) for non-agricultural uses.

EEC lb a.i./A					
Spray Drift		**Total for Dry Areas**		**Total for Semi-Aquatic Areas**	
Aerial Liquid	**Ground Liquid**	**Aerial Liquid**	**Ground Liquid**	**Aerial Liquid**	**Ground Liquid**
Ground spray application at 0.0375 lb a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf					
0.001875	0.000375	0.00225	0.00075	0.005625	0.004125
Ground spray Application at 0.225 lb a.i./acre for ornamental lawns and turf					
0.1125	0.00225	0.0135	0.0045	0.03375	0.02475
Ground spray broadcast at 1.437 lb a.i./acre for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites					
0.07185	0.01437	0.08622	0.02874	0.2155	0.15807

Table 29. Terrestrial plant EECs for indoxacarb (lbs a.i./A) for granular non-agricultural uses.

EEC lb a.i./A		
Spray Drift	**Total for Dry Areas**	**Total for Semi-Aquatic Areas**
Granular application rate of 0.1101 lb a.i./acre for commercial/institutional/industrial premises and equipment		

0	0.001101	0.01101
Granular and perimeter granule application rate of 0.44 lb a.i./acre for golf course turf, and household domestic dwellings		
0	0.004	0.044

5.0 Ecological Effects Characterization

Indoxacarb is highly toxic to fish and invertebrates. Three degradates have been identified (IN-JT333, IN-MP819, and IN-KN125) as having substantially greater toxicity to some aquatic taxa however this relationship varies across taxa. Where comparisons within a species can be made across the new TGAI (DPX-JW062), the old TGAI (DPX-MP062; a mixture of S and R enantiomers) and the refined R-enantiomer (DPX-KN127), the observed effects suggest similar toxicity across the compounds. Chronic effects were observed for both freshwater and estuarine/marine fish (e.g., growth, post-hatch survival). There is some uncertainty regarding the toxicity of parent and degradates to estuarine/marine fish, on an acute exposure basis the available studies produced non-definitive endpoints, but chronic effects on survival and growth were observed in a parent indoxacarb study and there are no available degradate chronic studies. Chronic exposure to benthic invertebrates in toxicity tests suggests that indoxacarb is much more toxic to these taxa than the two degradates of concern.

5.1 Aquatic Organisms

A summary of all acute and chronic aquatic toxicity effects studies for aquatic organisms and for indoxacarb and its degradates are presented in **Tables 30-39**.

Freshwater Fish

The current TGAI, DPX-JW062, is very highly toxic to rainbow trout with effects seen at doses as low as 0.352 mg a.i./L (MRID 48764601). Similarly, the older technical indoxacarb formulation DPX-MP062 is highly toxic to rainbow trout but only moderately toxic to carp. Comparison of acute endpoints across the DPX-JW062, DPX-MP062 (mixture of S and R enantiomers) and DPX-KN127 (refined R-enantiomer), based on the available rainbow trout studies, indicates that the endpoints are within an order of magnitude which suggests similar toxicity. The most sensitive fish species tested is channel catfish (LC_{50}=0.29 mg a.i.//L (MRID 44477211) which is the selected endpoint for quantitative assessment of risks.

Out of the degradates of the current technical mixture (Refined S-enantiomer, IN-KN128), DPX-KN125 and INJT333 were most highly toxic rainbow trout. DPX-KN125, a metabolite of JT-333 observed in an anaerobic soil metabolism study, is highly toxic with an LC_{50}=0.0098 mg a.i./L (MRID 49734502), compared to JT-333 (LC_{50}=0.024 mg a.i./L, MRID 44477216), but formation is only at 10.6%, and the exposure potential to fish is considered of minimal concern. This study was classified as supplemental quantitative, but there is uncertainty in the endpoint since the analytical recoveries are lower than suggested by the guidance. Degradate IN-MP819 had a non-definitive LC_{50}, and the degradates INU8E24 and UYG24 had were classified as slightly to practically non-toxic. For freshwater fish, the product formulation (based on the older technical), DPX-MP062 30WG, ranged from moderately to highly toxic or had a non-definitive endpoint (LC_{50}=0.71 mg a.i./L and 1.2 mg a.i./L and >0.187 mg a.i./L, MRIDs 49511511, 44477214 and 49511511). The IN-JT333 and IN-MP819 endpoints are used to calculate the toxicity ratios presented in for the TEQ EEC estimation.

On a chronic basis, the most sensitive endpoint was for the IN-JT333, (Fathead minnow NOAEC=0.00126 mg a.i./L, MRID 49566209), followed by the current technical formulation (NOAEC=0.0675 mg a.i./L, MRID 49566208). These effects were based on the most sensitive endpoint of post hatch survival. Like the effects noted within rainbow trout for acute studies with old and new technical formulations, there is less than an order of magnitude difference between the endpoints. This again suggests similar toxicity across the two technical formulations for chronic exposure, however there is uncertainty in the comparison due to the potential influence of dose spacing in the studies. Other effects on growth and survival were observed for DPX-MP062 technical mixture at a NOAEC of 0.15 mg a.i./L (MRID 44477228). Overall, due to the lack chronic toxicity data to the fathead minnow, this approach may be underestimating chronic risk if the fathead minnow is truly the more sensitive species (**Tables 30-31)**.

Table 30. Summary of acute freshwater fish effects data

Test Material	Organism	Endpoint[1] Summary	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S -enantiomer)			
DPX-JW062 Technical	Rainbow trout	96 hr LC_{50}=0.352 mg a.i./L	Guideline 850.1075 MRID 48764601 Supplemental Quantitative (Very highly toxic); Analytical recoveries were lower than those suggested by guideline
DPX-JW062 Technical	Carp	96 hr LC_{50}>0.320 mg a.i./L	Guideline 850.1075 MRID 44477212 Supplemental; Undissolved material in the analytical samples precluded an accurate assessment of the highest concentration.
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Rainbow Trout	96 hr LC_{50} = 0.65 mg a.i./L	Guideline 850.1075 MRID 44477209 Acceptable (Highly toxic)
DPX-MP062 Technical	Carp	96 hr LC_{50}=1.02 mg a.i./L	Guideline 850.1075 MRID 44487901 Supplemental (moderately toxic); Test

			species used not according to guideline
DPX-MP062 Technical	Bluegill Sunfish	96 hr LC_{50}=0.90 mg a.i./L	Guideline 850.1075 MRID 44477210 Acceptable (Highly toxic)
DPX-MP062 Technical	Channel Catfish	**96 hr LC_{50}=0.29 mg a.i./L***	Guideline 850.1075 MRID 44477211 Acceptable (Highly toxic)
Degradates of S-enantiomer (KN128)			
DPX-KN125	Rainbow Trout	96 hr LC_{50}=0.0098 mg a.i./L	Guideline 850.1075 MRID 49734502 Supplemental Quantitative (Highly toxic); Analytical recoveries were lower than those suggested by guideline
INJT333	Rainbow Trout	**96 hr LC50=0.024 mg a.i./L***	Guideline 850.1075 MRID 44477216 Acceptable (Highly toxic)
IN-MP819	Rainbow Trout	**96 hr LC50>0.368 mg a.i./L***	Guideline 850.1075 MRID 46022501 Acceptable (endpoint undefined, no mortality)
INU8E24	Rainbow Trout	96 hr LC50=46.5 mg a.i./L	Guideline 850.1075 MRID 49734511 Acceptable (Slightly toxic)
INUYG24	Rainbow Trout	96 hr LC50>115 mg a.i./L	Guideline 850.1075 MRID 49734508 Acceptable (Practically non-toxic)
Old TEP (14.7% S-Enantiomer, 4.3% R-Enantiomer Mixture)			
DPX-MP062 150SC	Rainbow Trout	96 hr LC_{50}>1.3 mg a.i./L	Guideline 850.1075 MRID 444747213 Supplemental; LC50 was not determined at the highest concentration and no inert control was included in the test.
DPX-MP062 30WG	Rainbow Trout	96 hr LC_{50}>0.187 mg a.i./L	Guideline 850.1075 MRID 49511511 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline
DPX-MP062 30WG	Rainbow Trout	96 hr LC_{50}=0.71 mg a.i./L	Guideline 850.1075 MRID 44477215 Acceptable (Highly toxic)
DPX-MP062 30WG	Bluegill Sunfish	96 hr LC_{50}=1.2 mg a.i./L	Guideline 850.1075 MRID 44477214 Acceptable (Moderately toxic)

Refined R-enantiomer (KN127) and Degradates of R-enantiomer			
DPX-KN127	Rainbow Trout	96 hr LC_{50}=0.394 mg a.i./L	Guideline 850.1075 MRID 44477218 Acceptable (Highly toxic)
DPX-KN124	Rainbow Trout	96 hr LC_{50}>0.0931 mg a.i./L	Guideline 850.1075 MRID 49734506 Supplemental Quantitative; Analytical Recoveries were lower than those suggested by the guideline

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs

Table 31. Summary of Chronic Freshwater Fish Effects Data

Test Material	Organism	Endpoint Summary[1]	MRID/ Study/Classification/Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Fathead Minnow	**NOAEC=0.0675 mg a.i./L*** LOAEC=0.129 mg a.i./L Based on post-hatch survival	Guideline 850.1400 MRID 49566208 Acceptable
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Rainbow Trout	NOAEC=0.15 mg a.i./L LOAEC=0.25 mg a.i./L Based on growth and survival	Guideline 850.1400 MRID 44477228 Supplemental; Variability measured in concentrations and the use of only two replicates per dose
Degradates of S-enantiomer (KN128)			
INJT333	Fathead Minnow	**NOAEC=0.00126 mg a.i./L*** LOAEC=0.00242 mg a.i./L Based on post-hatch survival	Guideline 850.1400 MRID 49566209 Acceptable
IN-MP819		**Estimated NOEC = 0.0849 mg a.i./L*** = (0.15 x|>3.68|)/0.65 = (DPX-MP062 Rainbow Trout NOEC x |IN-MP819 Rainbow trout LC50|) / DPX-MP062 Rainbow trout LC50	Note that the old technical was the only available material for doing the ACR Note that the available tox for MP819 is non-definitive

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs.

Estuarine/Marine Fish

For estuarine/marine fish only one acute and one chronic study were conducted with the older technical formulation (DPX-MP062) using the sheepshead minnow. For the acute study, the endpoint for the 96 hr LC_{50} was undetermined (LC_{50}>0.37 mg a.i./L, MRID 44477222). The study was classified as supplemental since the material was not tested to the maximum solubility in brackish water conditions. For the chronic study on DPX-MP062, the LOAEC=0.0417 mg a.i./L and was based on survival (44477226) (**Tables 32-33**). No new data were submitted for testing the new technical (DPX-JW062) on estuarine/marine fish.

Table 32. Summary of acute estuarine/marine fish effects data

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Sheepshead Minnow	**96 hr LC_{50}>0.37 mg a.i./L***	Guideline 850.1075 MRID 44477222 Supplemental; The test material was not tested to the maximum solubility under brackish water conditions. No mortality endpoint.
Degradates of S-enantiomer (KN128)			
INJT333		**Estimated NOEC = 0.014 mg a.i./L*** =(|>0.37|*0.024)/0.65 =(|DPX-MP062 Sheepshead Minnow LC50| * IN-JT333 Rainbow trout LC50) / DPX-MP062 Rainbow trout LC50)	Note that the available acute data for sheepshead is non-definitive No new technical data is available to revise the ACR
IN-MP819		**Estimated NOEC = 0.2095 mg a.i./L*** = (|>0.37|*|>3.68|)/0.65 = (|DPX-MP062 Sheepshead Minnow LC50| * |IN-MP819 Rainbow trout LC50|) / DPX-MP062 Rainbow trout LC50)	Note that the available data for MP819 and Old technical are non-definitive No new technical data is available to revise the ACR

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs.

Table 33. Summary of chronic estuarine/marine fish effects data.

Test Material	Organism	Endpoint Summary[1]	MRID/ Study/Classification/Comments
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Sheepshead Minnow	**NOAEC=0.0169 mg a.i./L** * LOAEC=0.0417 mg a.i./L Based on Survival	Guideline 850.1400 MRID 44477226 Acceptable
Degradates of S-enantiomer (KN128)			
INJT333		**Estimated NOEC = 0.2095 mg a.i./L*** = (0.0169 x 0.024)/0.65 = (DPX-MP062 Sheepshead Minnow NOEC x IN-JT333 Rainbow trout LC50) / DPX-MP062 Rainbow trout LC50	Note that new technical data is not available to revise the ACR
IN-MP819		**Estimated NOEC = 0.0096 mg a.i./L*** = (0.0169 x |>3.68|)/0.65 = (DPX-MP062 Sheepshead Minnow NOEC x |IN-MP819 Rainbow trout LC50|) / DPX-MP062 Rainbow trout LC50	Note new technical data is not available to revise ACR Note that data for MP819 is non-definitive

[1]**Asterisk (*) indicates the endpoints used in the calculations of TEQs.**

Freshwater Invertebrates

Out of all the degradates of the S-enantiomer KN128 in which studies were conducted, *Daphnia magna* were most sensitive to IN-MP819 (LC_{50}=0.064 mg a.i./L, MRID 46005801). The newer indoxacarb technical mixture was moderately toxic to *Daphnia carinata* on an acute basis (LC_{50}=2.94 mg a.i./L, MRID 44477219), however the study was not conducted on a recommended test species. The older technical formulation was highly toxic to *Daphnia magna* on an acute basis (96 hr LC_{50}=0.60 mg a.i./L, MRID 49734503). The 96-hour *Daphnia magna* endpoints for DPX-KN125, INJT333, and INU8E24 were non-definitive. However, the 48-hour endpoint (LC_{50}=30.7 mg a.i./L, MRID 49922101) for *Chironomus dilutus*, for INU8E24 was slightly toxic. The most sensitive species to the older technical formulation, 30WG was *Daphnia magna*, (LC_{50}=0.0324 mg a.i./L, MRID 48764602) compared to the *Hyalella azteca,* mayfly and stonefly.

On a chronic basis, two freshwater invertebrate studies were conducted, one with the current and one with the older technical mixture. The current technical formulation was more toxic to *Daphnia magna* compared to the old technical on a chronic basis (LOAEC=0.00585 mg a.i./L vs.

0.19 mg a.i./L respectively, MRIDs 49544310 and 44477225). The most sensitive endpoints were reductions in length and reproduction (**Table 34-35**).

Table 34. Summary of acute freshwater invertebrate effects data.

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Daphnia carinata	96 hr LC_{50}=2.94 mg a.i./L	Guideline 850.1010 MRID 44477219 Supplemental (moderately toxic) (not recommended test species)
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Daphnia magna	**96 hr LC_{50}=0.60 mg a.i./L***	Guideline 850.1010 MRID 44477219 Acceptable (highly toxic)
DPX-MP062 Technical	Daphnia pulex	48 hr LC_{50}>50 mg a.i./L (indoxacarb) Sublethal effects included instability in swimming position and decrease in spontaneous movement at the 1000 mg a.i./L treatment group.	MRID 44487903 **Currently Under Review**
Degradates of S-enantiomer (KN128)			
DPX-KN125	Daphnia magna	96 hr LC_{50} > 0.121 mg a.i./L	Guideline 850.1010 MRID 49734503 Supplemental Quantitative (highly toxic) Analytical recoveries were lower than those suggested by the guideline Mortality <50% at the highest test level
INJT333	Daphnia magna	**96 hr LC_{50}>0.029 mg a.i./L***	Guideline 850.1010 MRID 44477221 Supplemental; LC_{50} was not obtained and the solvent concentration in the test was not reported)
IN-MP819	Daphnia magna	**96 hr LC_{50}=0.064 mg a.i./L***	Guideline 850.1010 MRID 46005801 Acceptable (highly toxic)

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
INU8E24	Daphnia magna	96 hr LC_{50}>13.5 mg a.i./L	Guideline 850.1010 MRID 49734512 Acceptable
INU8E24	Chironomus dilutus	48 hr LC50=30.7 mg a.i./L	Guideline 850.1010 MRID 49922101 Acceptable (slightly toxic)
INU8E24	Daphnia magna	>113 mg a.i./L	MRID 49734509- **Currently Under Review**
Old TEP (14.7% S-Enantiomer, 4.3% R-Enantiomer Mixture)			
DPX-MP062 30WG	Daphnia magna	96 hr LC_{50}=0.0324 mg a.i./L	Guideline MRID 48764602 Acceptable (highly toxic)
DPX-MP062 30WG	Hyalella azteca	48 hr LC_{50}>160 µg a.i./L	Guideline 850.1010 MRID 49566202 Supplemental Qualitative (Non-guideline species was used; instability of the test substance indicates flow-through testing would have been more appropriate)
DPX-MP062 30WG	Mayfly	48 hr LC_{50}=7.77 µg a.i./L	Guideline 850.1010 MRID 49759901 Supplemental Quantitative (moderately toxic); The analytical recovery of indoxacarb was <70% of the initial concentrations at 24 and 48 hours indicating instability of the test compound.
DPX-MP062 30WG	Stonefly	48 hr LC_{50}=94.8 µg a.i./L	Guideline 850.1010 MRID 49566205 Supplemental Quantitative (slightly toxic); Non-guideline test species was used.
Refined R-enantiomer (KN127) and Degradates of R-enantiomer			
DPX-KN124	Daphnia magna	96 hr LC_{50}>0.106 mg a.i./L	Guideline 850.1010 MRID 49734504 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline.

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs.

Table 35. Summary of chronic freshwater invertebrate data.

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Daphnia magna	**NOAEC=0.00411 mg a.i./L*** LOAEC=0.00585 mg a.i./L Based on reduction in mean length	Guideline 850.1300 MRID 49544310 Supplemental Quantitative; Results of range finding test not included and maximum test concentrations did not reach limit of solubility.
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Daphnia magna	NOAEC=0.075 mg a.i./LLOAEC=0.19 mg a.i./L Based on reproduction	Guideline 850.1300 MRID 44477225 Acceptable
Degradates of S-enantiomer (IN-KN128)			
INJT333		**Estimated NOEC = 0.00020 mg a.i./L*** = (0.00411 x|>0.029|)/0.6 = (DPX-JW062 Daphnia magna NOEC x |IN-JT333 Daphnia magna LC50|) / DPX-MP062 Daphnia magna LC50	No new acute data for JW062 for D. magna Used old and new technical for the ACR Note that acute JT333 data is non-definitive
IN-MP819		Estimated NOEC = 0.00196 mg a.i./L* = (0.00411 x 0.064)/0.6 = (DPX-JW062 Daphnia magna NOEC x IN-MP819 Daphnia magna LC50) / DPX-MP062 Daphnia magna LC50	No new acute data for JW062 for D. magna Used old and new technical for the ACR

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs.

Two acute sediment toxicity studies on freshwater invertebrates were conducted. For the current technical mixture, *Chironomus dilutus*, has the most sensitive endpoint based on survival, LC_{50} = 720 µg a.i./kg (MRID 49827602). On a chronic basis, the most sensitive endpoint for the current technical mixture was also for *C. dilutus*, and was based on 28-day development rate (combined, male and female). Study MRID 49827602 quantified the formation of the degradates IN-JT333 and IN-MP819. As the nominal dose levels increased, the measured concentrations of the metabolite IN-MP819 increased from days 0 to 10, while formation of JT333 remained < LOD in water (**Tables 36)**.

Table 36. Summary of freshwater invertebrate sediment effects data.

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Subchronic Studies			
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Hyalella azteca	10-day study Mean measured sediment Survival and Dry Weight: LC_{50}> 1030 µg a.i./kg NOAEC=1030 µg a.i./kg OC normalized Survival and Dry Weight LC_{50} > 74 mg a.i./kg OC NOAEC=74 mg a.i./kg Estimated Porwater Survival and Dry weight: LC_{50}>201 ng a.i./kg NOAEC=201 mg a.i./kg	Guideline 850.1735 MRID 49827603 Acceptable
	Chironomus dilutus	10-day study Most sensitive endpoint survival *Indoxacarb Koc=5125* Mean measured sediment **Survival: LC_{50}=720 µg a.i./kg** NOAEC=327 µg a.i./kg Dry Weight: LC_{50}=1140 µg a.i./kg NOAEC=790 µg a.i./kg OC normalized Survival LC_{50}=51.1 µg a.i./kg NOAEC=23 µg a.i./kg Dry Weight: LC_{50}=81.4 µg a.i./kg NOAEC=56 µg a.i./kg Estimated Porewater **Survival LC_{50}=140 ng a.i./L** NOAEC=63.8 ng a.i./L Dry Weight: LC_{50}=222.44 ng a.i./L NOAEC=154.15 ng a.i./L	Guideline 850.1735 MRID 49827602 Acceptable
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Chironomus tentans	10 day LC_{50}> 30 µg/g OC	44477220 **Currently Under Review**
Degradates of S-enantiomer (IN-KN128)			
INJT333		Estimated LC50 =71.63 mg a.i./L = (DPX-JW062 Chiro LC50* IN-	Not included in calculation of RQs because estimated endpoint is 100x higher than indoxacarb.

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
		JT333 Chiro NOAEC) / DPX-JW062 Chiro NOAEC)	
IN-MP819		Estimated LC50 =64,315 mg a.i./L = (DPX-JW062 Chiro LC50* IN-MP819 Chiro NOAEC) / DPX-JW062 Chiro NOAEC)	Not included in calculation of RQs because estimated endpoint is 10000x higher than indoxacarb.
Chronic Studies			
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Chironomus dilutus	**Most sensitive endpoint: 28 day development rate (combined, male, female)** **TWA Bulk Sediment (µg TRR/kg)** **NOAEC=0.965** LOAEC=1.78 TWA OC Normalized Sediment (µg TRR/g OC) NOAEC=0.0402 LOAEC= 0.0742 **TWA Pore Water (µg a.i./L)** **NOAEC= 0.548*** LOAEC=1.69 TWA Overlying Water (µg a.i./L) NOAEC=0.839 LOAEC=2.65	OECD Guideline 219 MRID 49321503 Acceptable
DPX-JW062 Technical	Chironomus dilutus	Most sensitive endpoint: 28 day emergence TWA Bulk Sediment (µg TRR/kg) 28-day emergence: NOAEC=1.47 LOAEC=3.35 TWA OC Normalized Sediment (µg TRR/g OC) 28 day emergence: NOAEC=0.113 LOAEC=0.258 TWA Pore Water (µg a.i./L) 28-day emergence: NOAEC=0.500 LOAEC=1.18 TWA Overlying Water (µg a.i./L) 28-day emergence:	OECD Guideline 219 MRID 49735301 Supplemental Quantitative; There were statistically significant solvent effects, for combined and female development rate, which could confound treatment related effects for these endpoints making them unreliable for statistical analysis)

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
		NOAEC=0.875 LOAEC=1.78	
DPX-JW062 Technical	Chironomus riparius	Development rate NOAEC=26.2 µg DPX JW-062L	45333702 **Currently Under Review**
Degradates of S-enantiomer (IN-KN128)			
INJT333	Chironomus riparius	Most sensitive endpoint was development rate with an NOAEC=9.87 µg a.i./g OC	45333701 **Currently Under Review**
IN-MP819	Chironomus dilutus	**Based on emergence rate, survival, male:female ratio and development rate** Mean measured sediment **NOAEC= 86.2 mg TRR/kg** LOAEC>86.2 mg TRR/kg OC normalized NOAEC=3320 mg TRR/kg LOAEC>3320 mg TRR/kg Mean measured Porewater **NOAEC=0.599 mg TTR/L** LOAEC>0.599 mg TRR/L Overlying Water NOAEC=0.599 mg TRR/L LOAEC>0.599 mg TRR/L	OECD Guideline 218 MRID 49827604 Acceptable

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs.

Estuarine/Marine Invertebrates

On an acute basis, the current technical formulation DPX-JW062 is highly toxic to estuarine/marine shrimp with a 96 hr LC_{50}=0.366 mg total a.i./L (MRID 49511508). Previous studies indicate that the older technical formulation is also highly toxic to both the mysid (LC_{50} = 0.0542 mg a.i./L, MRID 44477223) and mollusk (LC_{50}=0.203 ppm a.i, MRID 44477224). The degradate IN-JT333 of the S-enantiomer KN-128 (current technical formulation), was highly toxic to the estuarine/marine shrimp on an acute basis (LC_{50}=0.069 mg a.i./L, 49511507), but non-definitive for INKG433 on acute basis (LC_{50}>0.0165 µg a.i./L, MRID 49511510). Both studies were classified as supplemental quantitative due to low analytical recoveries. The only formulation tested on estuarine/marine shrimp on an acute basis was DPX-MP062 30WG and the study was again classified as supplemental quantitative due to low analytical recoveries and an indefinitive endpoint. One chronic toxicity study was conducted on the mysid for the older technical for estuarine/marine invertebrates. The LOAEC=0.0407 mg a.i./kg and was based on survival (MRID 49827601).

One estuarine/marine invertebrate sediment study was conducted with the current technical formulation (DPX-JW062). The 96 hr LC_{50} was indefinitive (LC_{50}>0.474 mg a.i./kg, MRID 49876201) (**Tables 37-39**).

Table 37. Summary of acute Effects data for estuarine/marine invertebrates

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	Mysid Shrimp (*Americamysis bahia*)	96 hr LC_{50}=0.366 mg a.i./L	Guideline 850.1035 MRID 49511508 Supplemental Quantitative (highly toxic) Analytical recoveries were lower than those suggested by the guideline
DPX-JW062 Technical	Mysid Shrimp (*Americamysis bahia*)	96 hr LC_{50}>0.126 mg a.i./L	Guideline 850.1035 MRID 49511509 Supplemental Quantitative Analytical recoveries were lower than those suggested by the guideline
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			
DPX-MP062 Technical	Mysid	**96 hr LC_{50}=0.0542 mg a.i./L***	Guideline 850.1035 MRID 44477223 Acceptable (Very highly toxic)
DPX-MP062 Technical	Mollusk	96 hr LC_{50}=0.203 ppm a.i	Guideline MRID 44477224 Acceptable (highly toxic)
Degradates of S-enantiomer (KN128)			
INJT333	Mysid Shrimp (*Americamysis bahia*)	**96 hr LC_{50}=0.069 mg a/L***	Guideline 850.1035 MRID 49511507 Supplemental Quantitative (highly toxic); Analytical recoveries were lower than those suggested by the guideline
INKG433	Mysid Shrimp (*Americamysis bahia*)	96 hr LC_{50} > 0.0165 µg a.i./L	Guideline 850.1035 MRID 49511510 Supplemental Quantitative Unstable test material and concentration recoveries were

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
			below the suggested acceptable guidelines
IN-MP819		**Estimated LC50 = 0.00578 mg a.i./L*** = (DPX-MP062 Mysid LC50* IN-MP819 Daphnia magna LC50) / DPX-JW062 Daphnia magna LC50)	
Product Formulations (Based on Old Technical)			
DPX-MP062 30WG	Mysid Shrimp (*Americamysis bahia*)	96 hr LC_{50}>0.217 mg a.i./L	Guideline 850.1035 MRID 49544309 Supplemental Quantitative Unstable test material and concentration recoveries were below the suggested acceptable guidelines

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs

Table 38. Summary of chronic effects data for estuarine/marine invertebrates

Test Material	Organism	Endpoint Summary[1]	MRID/ Study/Classification/Comments
Old Technical Formulation (Mixture of S and R Enantiomers)			
DPX-MP062 Technical	Mysid	**NOAEC=0.0184 mg a.i./kg*** LOAEC=0.0407 mg a.i./kg Based on survival	Guideline 850.1300 MRID 49827601 Acceptable
Degradates of S-enantiomer (KN128)			
INJT333		**Estimated NOEC = 0.05432 mg a.i./L*** = (DPX-MP062 Mysid NOAEC * IN-JT333 Mysid LC50) / DPX-JW062 Mysid LC50)	
IN-MP819		**Estimated NOEC =0.00196 mg a.i./L*** = (DPX-JW062 Daphnia magna NOEC * IN-MP819 Daphnia magna LC50) / DPX-JW062 Daphnia magna LC50)	

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs

Table 39. Summary of acute sediment effects data for estuarine/marine invertebrates

Test Material	Organism	Endpoint Summary[1]	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	*Leptocheirus plumulosus*	Mean measured sediment 96 hr LC_{50}>0.474 mg a.i./kg OC normalized mean measured sediment 96 hr LC_{50}>34 mg a.i./kg OC Porewater concentrations 96 hr LC_{50}>92.48 ng a.i./kg	Guideline 850.1740 MRID 49827601 Acceptable

[1]Asterisk (*) indicates the endpoints used in the calculations of TEQs

Aquatic Plants

The only vascular aquatic plant study available was conducted with *Lemna gibba* exposed to the older DPX-MP062 technical formulation. The endpoint for *Lemna* was non-definitive and the study was classified as supplemental due to the instability of the test material in solution. For non-vascular plants effects were seen only for *Selenastrum capricornutum* with an EC_{50}=1215 mg a.i./L and a NOAEC=428 mg a.i./L for reductions in population growth. Effects were also observed for non-vascular plant species *Pseudokirchneriella subcapitata* for effects on yield, with a NOAEC of 6.9 mg a.i./L IN-UYG24 and 6.3 mg a.i./L for IN-U8E24.

Effects on non-vascular aquatic plants were not seen at the maximum tested dose levels and indoxacarb application rates (**Table 40**).

Table 40. Summary of the vascular and non-vascular plant effects studies

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Current TGAI (95% Refined S-enantiomer)			
DPX-JW062 Technical	*Pseudokirchneriella subcapitata*	IC_{50}>0.177 mg a.i./L NOAEC=0.177 mg a.i./L LOAEC>0.177 mg a.i./L No endpoints effected	Guideline 850.4500 MRID 49544322 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline.
Old TGAI (75% S-Enantiomer, and 25% R-enantiomer Mixture)			

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
DPX-MP062 Technical	*Selenastrum capricornutum*	NOAEC>110 ppb a.i	Guideline 850.4500 MRID 44491702 Acceptable; This study is scientifically sound and fulfills the guideline requirements for a Tier I aquatic plant toxicity test.
DPX-MP062 Technical	*Skeletonema costatum*	EC_{50}=1215 mg a.i. /L (153 g a.i./hectare) NOAEC=428 mg a.i./L LOAEC=891 mg a.i./L (Visually determined, effects on population growth).	Guideline 850.4500 MRID 44477231 Acceptable; NOAEC could not be determined due to significant reductions in growth at all concentrations.
DPX-MP062 Technical	*N. pelliculosa*	Test concentration over 20 times the maximum application rate, does not inhibit growth by 50% or more	Guideline 850.4500 MRID 44477232 Acceptable; Fulfills the requirements for Tier I algal toxicity test. 120 h growth was not inhibited when exposed to test material at >20 times the concentration (1.68 ppm a.i) if DPX-MP062 is applied at the maximum label rate.
DPX-MP062 Technical	*Anabaena flow-aquae*	Test concentration over 20 times the maximum application rate does not inhibit growth by 50% or more	Guideline 850.4500 MRID 4447233 Acceptable
DPX-MP062 Technical	*Lemna gibba*	EC_{50}>0.084 mg a.i./L NOAEC=0.084 mg a.i./L	Guideline 850.4500 MRID 44477230 Supplemental; Test material unstable in solution as both the treatment and abiotic control solutions did not contain detectable amounts of the test material.
Degradates of S-enantiomer (KN128)			
DPX-KN125	*Pseudokirchneriella subcapitata*	IC_{50}>0.149 mg a.i./L NOAEC=0.149 mg a.i./L LOAEC>0.149 mg a.i./L No endpoints effected	Guideline 850.4500 MRID 49734501 Supplemental Quantitative; Analytical

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
			recoveries were lower than those suggested by the guideline.
IN-U8E24	*Pseudokirchneriella subcapitata*	IC_{05}=7.07 mg a.i./L IC_{50}=25.3 mg a.i./L NOAEC=6.97 mg a.i./L LOAEC=14.4 mg a.i./L Most sensitive endpoint: Yield	Guideline 850.4500 MRID 49544323 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline.
IN-UYG24	*Pseudokirchneriella subcapitata*	IC_{05}=15.5 mg a.i./L IC_{50}=78.8 mg a.i./L NOAEC=6.30 mg a.i./L LOAEC=12.6 mg a.i./L Most sensitive endpoint: Yield and Area Under the Curve	Guideline 850.4500 MRID 49734507 Acceptable
Product Formulations (Based on Old Technical)			
DPX-MP062 30WG	*Pseudokirchneriella subcapitata*	IC_{05}= N/A IC_{50}>0.189 mg a.i./L NOAEC=0.0800 mg a.i./L LOAEC>0.189 mg a.i./L Endpoints affected are Yield, Growth Rate, Area Under Curve	Guideline 850.4500 MRID 49544323 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline.
Refined R-enantiomer (KN127) and Degradates of R-enantiomer			
DPX-KN124	*Pseudokirchneriella subcapitata*	IC_{05}= Not calculable IC_{50}>0.163 mg a.i./L NOAEC=0.163 mg a.i./L LOAEC>0.163 mg a.i./L No endpoints effected	Guideline 850.4500 MRID 49734505 Supplemental Quantitative; Analytical recoveries were lower than those suggested by the guideline.

5.2 Terrestrial Organisms

A summary of avian, mammalian, and terrestrial plant and invertebrate toxicity effects data are presented in the following tables. Indoxacarb is acutely toxic to birds and mammals, and is chronically toxic to mammals. In birds, the degradate IN-JT333 is of limited acute toxicity compared to the parent indoxacarb, but IN-JT333 is more acutely toxic to mammals than the parent. Risk estimation for mammals relied upon IN-JT333 toxicity and exposure estimates. Indoxacarb and its degradates are highly toxic to honeybees on an acute oral and contact basis for adult honeybees, and acute and chronic basis for honeybee larvae. Several submitted Tier II honeybee toxicity studies were evaluated and the Agency determined that they were not suitable for quantitative use for various reasons (including having a single dose and not testing up to maximum labeled or estimated exposure rates), however their results indicate that colony level effects may be occurring in some studies. Indoxacarb appears to be similarly toxic to bumblebee on an acute exposure basis. There is limited toxicity to terrestrial plants.

Birds and Mammals

Birds

Avian toxicological endpoints are presented in **Table 41-42.** On an acute basis, indoxacarb is "moderately toxic" to avian species, with an LD_{50}=98 mg a.i./kg DPX-MP062 (bobwhite quail). This acute oral endpoint serves as the toxicological endpoint in this risk assessment. Indoxacarb is again moderately toxic to avian species on a subacute dietary basis with an LC_{50}=808 mg a.i./kg-diet DPX-MP062 (bobwhite quail). To compare DPX-MP062 and IN-JT333 on an equal basis, the avian endpoints for bobwhite quail on an acute and chronic basis were converted to the molar equivalent of "indoxacarb parent" to allow for unbiased comparison among toxicity endpoints (**Table 41**). Birds were more sensitive to the parent DPX-MP062 compared to the degradate of the S-enantiomer (IN-JT333). IN-JT333 is only slightly toxic to avian species on an acute basis. A dietary subacute avian study was not submitted for IN-JT333. The most recent acute oral study on a passerine species (zebra finch) was submitted for the current TGAI refined *S*-enantiomer. However, since this was the only avian study on a passerine for the current material, it is difficult to make comparisons across degradates. On a chronic basis, avian effects studies were performed with the parent in mallard ducks and bobwhite quail. The lowest NOAEC was for bobwhite quail, which will serve as the endpoint in this risk assessment (NOAEC=144 mg/kg-diet with DPX-MP062, MRID 444772205). The endpoint is based on reduced body weight in females and reduction in food consumption. A chronic toxicity study in the mallard resulted in a NOAEC=200 mg a.i./kg diet with DPX-MP062. The study was classified as supplemental due to the percentage of normal hatchlings of eggs laid, and viable embryos in the control group was low. The study suggested that this could be due to the inadequate test conditions in the incubator/hatcher. The final reproductive study was in the mallard which resulted in a NOAEC=720 mg a.i./kg with DPX-MP062, but no effects were observed at the highest test concentration. In birds, there are not sufficient toxicological data to determine if the toxicity of indoxacarb is due to the product toxicity of KN-128 alone or in combination with the other the *R*-enantiomer.

Table 41. Summary of acute avian effects data[1]

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Current TGAI (Refined *S*-Enantiomer, 95% *S*-enantiomer)			
DPX-JW062 Technical	Zebra Finch	LD_{50}=315.5 mg a.i./kg bw	Guideline 850.2100 MRID 49599602 Acceptable (highly toxic)
Old TGAI (75% S-Enantiomer and 25% *R*-Enantiomer)			
DPX-MP062 Technical	Northern Bobwhite Quail	**LD_{50}=98 mg a.i./kg bw**	Guideline 850.2100 MRID 44477201 Acceptable (highly toxic)
DPX-MP062 Technical	Northern Bobwhite Quail	**LC_{50}=808 mg a.i./kg-diet**	Guideline 850.2200 MRID 44491701 Acceptable (moderately toxic)
DPX-MP062 Technical	Mallard Duck	LC_{50}>5620 mg a.i./kg-Diet	Guideline 850.2200 MRID 44477204 Acceptable (practically non-toxic)
Degradates of *S*-enantiomer (KN128)			
IN-JT333	Northern Bobwhite Quail	LD_{50}=1618 mg a.i./kg bw[2]	Guideline 850.2100 MRID 44477203 Acceptable (slightly toxic)

[1] **BOLD indicates endpoint used in RQ calculations**

[2] Molar equivalent for this endpoint based on both the molar weights of Indoxacarb DPX-MP062 and IN-JT333 is 1817.8 mg a.i.kg/bwt

Table 42. Summary of chronic avian effects data

Test Material	Organism	Summary	MRID/ Study/Classification/Comments
Current TGAI (Refined *S*-Enantiomer, 95% *S*-enantiomer)			
DPX-JW062 Technical	Mallard	NOAEC=200 mg a.i./kg diet LOAEC=1000 mg a.i./kg diet Based on reduction in number of normal hatchlings and 14-day old survivors	Guideline 850.2300 MRID 44477208 Supplemental; The percentage of normal hatchlings of eggs laid, eggs set, and viable embryos in the control group was unacceptably low. This may have been due to inadequate conditions of the test, particularly the incubator and/or the hatcher. It was already reported by the authors that an accident involving the incubator resulted in the destruction of some eggs from Lots L and M.
Old Technical Formulation (Mixture of *S* and *R* Enantiomers)			
DPX-MP062 Technical	Northern Bobwhite	**NOAEC=114 mg a.i./kg diet** LOAEC=720 mg a.i./kg diet Based on adult body weight and food consumption of exposure	Guideline 850.2300 MRID 44477205 Acceptable
DPX-MP062 Technical	Mallard	NOAEC=720 mg a.i./kg diet LOAEC> 720 mg a.i./kg-diet No endpoints affected	Guideline 850.2300 MRID 44477206 Acceptable

[1] **BOLD indicates endpoint used in RQ calculations**

Mammals

For the purposes of this risk assessment, EFED used the available mammalian data on rodents as surrogates for mammalian wildlife. The most sensitive acute and chronic toxicity reference values for mammals are summarized in **Table 43**. To compare DPX-MP062 to IN-JT333 on an equal basis, the mammalian endpoint for rats on an acute basis was converted to the molar equivalent of the “indoxacarb parent” to allow of unbiased comparisons among toxicity endpoints. Unlike birds, the degradate IN-JT333 is more acutely toxic to mammals compared to the parent (LC_{50}=39 mg a.i./kg bw for IN-JT333 and 43.8 mg a.i./kg bw in indoxacarb units). In this risk assessment, the toxicity of indoxacarb to mammals on an acute oral basis was assessed using the most sensitive endpoint (179 mg a.i./kg bw, MRID 44477115) for the for DPX-JW062, the current parent form. On a chronic basis, indoxacarb and its degradates were highly toxic to mammals with a developmental NOAEC=40 mg a.i./kg diet (MRID 44477139). Hemolytic effects were also observed as low as 20 mg a.i./kg on a subacute dietary basis in both male and female rats (MRID 44477132), but how well these effects translate into risk concerns for survival and reproduction in the wild in uncertain. The mammalian reproduction endpoint selected for this study is from the 15-day mammalian developmental study of NOAEC=40 mg a.i./kg diet (MRID 44477139) and is based on reduced fetal body weights. Both avian and mammalian acute and chronic endpoints have not changed since the most recent Section 3 Assessment (US EPA 2016) (**Table 43**).

Table 43. Summary of acute mammalian effects data[1]

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Current TGAI (Refined *S*-Enantiomer, 95% *S*-enantiomer)			
DPX-JW062 Technical	Rat-Acute Oral	**Female LD_{50}=179 mg a.i./kg bw** Male LD_{50} >843 mg a.i./kg bw	Guideline 870.1100 MRID 44477115
Old Technical Formulation (Mixture of *S* and *R* Enantiomers)			
DPX-MP062 Technical	Rat-Acute Oral	Female LD_{50}=268 mg a.i./kg bw Male LD_{50} =1730 mg a.i./kg bw Combined LD_{50}<1000 mg a.i./kg bw	Guideline 870.1100 MRID 44477113
DPX-MP062 Technical	Rat-Inhalation	LC_{50}>5.5 mg a.i./kg (limit test)	Guideline 870.1300 MRID 44477120
Degradates of *S*-enantiomer (KN128)			
IN-JT333	Rat-Acute Oral	**Female LD_{50}=39 mg a.i/kg bw[2]** Male LD_{50} =52 mg a.i./kg bw	Guideline 870.1100 MRID 44477117 Highly toxic
IN-KG433	Rat-Acute Oral	Female LD_{50}=174 mg a.i./kg bw Male LD_{50} >2000 mg a.i./kg bw	Guideline 870.1100 MRID 44477116

[1] **BOLD indicates endpoint used in RQ calculations**

[2] Molar equivalent for this endpoint based on both the molar weights of Indoxacarb DPX-MP062 and IN-JT333 is 43.8 mg a.i./kg bw.

Table 44. Summary of chronic mammalian effects data

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Current TGAI (Refined *S*-Enantiomer, 95% *S*-enantiomer)			
DPX-JW062 Technical	Rat-15 day developmental	Developmental toxicity in offspring: **NOAEC=40 mg a.i./kg diet** LOAEC=80 mg a.i./kg diet (Based on reduced fetal weight)	Guideline 870.3550 MRID 44477139 Acceptable
DPX-JW062 Technical	Sub-chronic Oral Toxicity 90 days	Male NOAEC=20 mg a.i./diet Female NOAEC=8 mg a.i./kg diet Female LOAEC=20 mg a.i./kg diet Based on hemolytic effects	Guideline 870.3100 MRID 44477132
KN 128	Rat-Sub-Chronic Oral toxicity 90 day	Male NOAEC=10 mg a.i./kg-diet Female NOAEC <10 mg a.i./kg -diet Based on hemolytic effects	Guideline 870.3100 MRID 44477129 Acceptable

[1] **BOLD** indicates endpoint used in RQ calculations

Terrestrial Plants

There were no effects to terrestrial plants at application rates tested in the study. However, the studies did not test up to the maximum application rate of indoxacarb of 1.437 lbs a.i./acre for non-agricultural uses. There were no effects on terrestrial plants at doses tested in the studies up to 0.12 lbs a.i./acre (**Table 45**) which is slightly above the maximum single application rate for agricultural uses (0.1125 lbs a.i./A).

Table 45. Summary of effects data for terrestrial plants

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Product Formulations (Based on Old Technical)			
DPX-MP062 150SC	Monocots: Corn (*Zea may),* Oat (*Avena sativa),* Onion (*Allium cepa*), Perennial Ryegrass (*Lolium perenne)* Dicots: *Cucumber (Cucumis sativus), Oilseed rape (Brassica napus); Pea (Pisum sativum) Soybean (Glycine max) Sugarbeet (Beta vulgaris) Tomato (Lycopersicon esculentum)*	**Vegetative Vigor:** Monocot and Dicot: NOAEC=0.090 lb a.i./A Most sensitive could not be determined	Guideline 850.4100 MRID 49551402; Supplemental Quantitative. No effects at the highest test concentration which is below the maximum labeled rate (1.437 lbs a.i./A). However, the study meets the guideline requirements for labeled

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
			rates up to 0.090 lbs a.i./A.
DPX-MP062 30WG	Monocots: Corn (*Zea may),* Oat (*Avena sativa),* Onion (*Allium cepa*), Perennial Ryegrass (*Lolium perenne)* Dicots: *Cucumber (Cucumis sativus), Oilseed rape (Brassica napus); Pea (Pisum sativum) Soybean (Glycine max) Sugarbeet (Beta vulgaris) Tomato (Lycopersicon esculentum)*	**Seedling Emergence:** Monocot and Dicot: NOAEC=0.11 lb a.i./A EC_{25}>0.11 lb a.i./A Most sensitive could not be determined	Guideline 850.4100 MRID 49551401 Supplemental Quantitative; No effects at the highest test concentration which is below the maximum labeled rate (1.437 lbs a.i./A). However, the study meets the guideline requirements for labeled rates up to 0.11 lbs a.i./A.
	Monocots: Corn (*Zea may),* Oat (*Avena sativa),* Onion (*Allium cepa*), Perennial Ryegrass (*Lolium perenne)* Dicots: *Cucumber (Cucumis sativus), Oilseed rape (Brassica napus); Pea (Pisum sativum) Soybean (Glycine max) Sugarbeet (Beta vulgaris) Tomato (Lycopersicon esculentum)*	**Vegetative Vigor:** Monocot: EC_{25}>0.11 lb a.i./A NOAEC=0.11 lb a.i./A (oat, onion, ryegrass), 0.12 (corn) Dicot: EC_{25}>0.11 lb a.i./A NOAEC=0.11 lb a.i./A (cucumber, oilseed rape, pea, tomato), 0.12 (soybean, sugarbeet) Most sensitive could not be determined	Guideline 850.4100 MRID 49551403 Supplemental Quantitative; No effects at the highest test concentration which is below the maximum labeled rate (1.437 lbs a.i./A). However, the study meets the guideline requirements for labeled rates up to 0.11 lbs a.i./A.

Terrestrial Invertebrates

The primary species of focus in this section of the risk assessment is the honey bee and reflects the dominant role this species maintains in providing managed pollination services for agricultural crops throughout the U.S. It also reflects the availability of standardized methods for estimating exposure and effects on *A. mellifera*. As such, this assessment considers a variety of measures of effects for quantifying risk to honey bees, which differ according to the level of biological organization being assessed. At the Tier I (organism) level, measures of effects include:

- The acute contact LD50 to adult worker bees,
- The acute oral LD50 to adult worker bees
- The chronic (10-d) oral NOAEL for adult worker bees, and

- The chronic (21-d) NOAEL for larval bees.

Although the focus of this risk assessment is on the honey bee, the Agency recognizes that numerous other species of bees occur in North America and that these non-*Apis* bees have ecological and in some cases, commercial importance. For example, several species of non-*Apis* bees are commercially managed for their pollination services, including bumble bees (*Bombus spp.)*, leaf cutting bees (*Megachile rotundata*), alkali bees (*Nomia melanderi*), blue orchard bees (*Osmia lignaria)*, and the Japanese horn- faced bee (*Osmia cornifrons*). Importantly, a growing body of information indicates native bees play an important role in crop and native plant pollination, besides their overall ecological importance via maintaining biological diversity. Although standard methods are currently not available to quantitatively assess exposure and effects to non-*Apis* bees, this assessment relies upon the published data on the effects of indoxacarb to *Apis* bees as a surrogate for non-*Apis* bees.

Laboratory studies are available for honey bee larvae and adults (**Table 46**). Based on these data indoxacarb is classified as very highly toxic (i.e., LD_{50} <2 ug a.i./bee) to larvae and adults on an acute exposure basis. In an acute toxicity study with DPX-JW062 the acute oral adult LC_{50} =0.204 µg a.i./bee (MRID 49366004) and acute contact LC_{50} = 0.068 µg a.i./bee. There were no data submitted to evaluate a chronic (10-d) oral exposure route for adult worker bees. For larvae, there are not data available to evaluate exposure to the technical, however in a 72-hour acute single dose study with KN-128 150EC, the LD_{50} was 18.1 µg/larva (MRID 49551404). An additional 10-day larval feeding study with KN-128 150EC was submitted and yielded a more sensitive LD_{50} (0.0403 ug a.i./L) and a NOAEL of 0.0078 ug a.i./larvae based on 7.5% mortality at 0.015 ug a.i./larvae. However, this exposure is considered similar to the chronic exposure represented by the available 22-day chronic larval toxicity studies which yielded a NOAEL of 0.0168 µg/larva (MRID 50182701), based on emergence. The latter will be used for quantitative evaluation of risks to larvae from chronic exposure. A suite of studies from MRID 44487904 were conducted with the JE874, a degradate of the older technical indoxacarb formulation. Overall, endpoints were non-definitive, and this degradate was classified as practically non-toxic to honeybees. The study was classified as supplemental due to too many unreported data points and unexplained mortalities in the 50 µg a.i./bee group, whereas no mortalities occurred in higher concentrations.

Table 46. Summary of Tier I Honeybee Studies

Test Material	Organism, Life Stage	Exposure Route (Duration)	Summary	Guideline #, MRID, Classification, Comments
Current Technical Formulation (Refined S-Isomer)				
DPX-JW062 Technical	Honeybee Adult	Acute Contact Toxicity Test	**Contact: LD_{50}=0.068 µg a.i./bee**	Non-guideline MRID 49366004 Acceptable (Highly toxic)

Test Material	Organism, Life Stage	Exposure Route (Duration)	Summary	Guideline #, MRID, Classification, Comments
DPX-JW062 Technical	Honeybee Adult	Acute Contact	LD_{50}=0.118 µg a.i./bee	Non-guideline MRID 44487904 Supplemental; Lack of information in testing design
DPX-JW062 Technical	Honeybee Adult	Acute Contact	LD_{50}=0.18 µg a.i./bee	Non-guideline MRID 44477234 Acceptable
DPX-JW062 Technical	Honeybee Adult	Acute Contact	LD_{50}=15.12 µg a.i./bee	Non-guideline MRID 44487904 Supplemental; Lack of information in testing design
DPX-JW062 Technical	Honeybee Adult	Acute Oral Toxicity Test	**Oral: LD_{50} = 0.204 µg a.i./bee**	Non-guideline MRID 49366004 Acceptable (Highly toxic)
DPX-JW062 Technical	Honeybee Adult	Acute Oral	LD_{50}=37.18 µg a.i./bee	Non-guideline MRID 44487904 Supplemental; Some unreported data points
DPX-JW062 Technical	Honeybee Adult	Acute Oral	LD_{50}= 18.52 µg a.i./bee	Non-guideline MRID 44487904 Supplemental; Some unreported data points
DPX-JW062 Technical	Honeybee Adult	Honeybee Acute Dietary LC_{50} test	LC_{50}>1000 ppm	Non-guideline MRID 44477235 Acceptable
DPX-JW062 Technical	Honeybee Larvae	Chronic 22-day (Repeat Dose) Toxicity Test with Larvae	Day 22 ED_{50}: 0.0255 µg a.i./larva Day 22 EC_{50}: 0.659 mg a.i./kg diet **Day 22 NOAEL: 0.0168 µg a.i./larva** Day 22 NOAEC: 0.434 mg a.i./kg diet Most sensitive endpoints: Emergence	Non-guideline MRID 50182701 Acceptable
Product Formulations (Based on Old Technical)				
DPX-MP062 30WG	Honeybee Adult	Acute Oral and Contact	Oral: LD_{50}=0.478 µg a.i./bee Contact: LD_{50}=0.566 µg a.i./bee	Non-guideline MRID 49511505 Acceptable (Highly Toxic)

Test Material	Organism, Life Stage	Exposure Route (Duration)	Summary	Guideline #, MRID, Classification, Comments
Product Formulations (Based on New Technical)				
KN-128 150EC	Honeybee Adult	Acute Oral and Contact Toxicity Test	Oral: LD_{50}=0.528 µg a.i./bee Contact LC_{50}=1.5 µg a.i./bee	Non-guideline MRID 49511502 Acceptable (Highly Toxic)
KN-128 150EC	Honeybee Larvae	72-hour toxicity acute single dose	**LD_{50}=18.1 µg a.i./larva** LD_{50}=544 mg a.i./kg diet	Non-guideline MRID 49551404 Acceptable
KN-128 150EC	Honeybee Larvae	Chronic 10-day larval continuous feeding study	LD_{50}=0.0403 µg a.i./larva Endpoints: Mortality sublethal effects observed, apathetic bees, moribund and cramping bees	Non-guideline MRID 49366002 Supplemental; Does not currently follow an available agency approved guideline
KN-128 150EC	Honeybee Larvae	Chronic 22-day (Repeat Dose) Toxicity Test with Larvae	Day 22 ED50: 0.0434 µg a.i./larva (0.268 µg EC/larva) Day 22 EC50: 1.13 mg a.i./kg diet (6.96 mg EC/kg diet) Day 22 NOAEL: 0.0279 µg a.i./larva (0.172 µg EC/larva) Day 22 NOAEC: 0.726 mg a.i./kg diet (4.48 mg EC/kg diet) Most sensitive endpoint: Emergence	Non-Guideline MRID 50182702 Acceptable
JE874 – Degradate of Old Technical				
JE874-247	Honeybee		Oral: 24 and 48 hour LD_{50}: >153.0 µg/bee	44487904 Supplemental Too many data points were unreported and there was an unexplained 36.7% mortality in the 50 ug/bee concentration group where no mortalities occurred in the higher concentrations.
JE874-247	Honeybee		Oral: LD_{50} > 400 µg/bee	
JE874-28	Honeybee		Oral: LD_{50} > 110.2 µg/bee	
JE874-28	Honeybee		Contact: LD_{50} = 288.69 µg/bee;	
JE874-244	Honeybee		Oral: LD_{50} > 133.3 µg/bee	
JE874-244	Honeybee		Contact: LD_{50} > 400 µg/bee	
JE874-224	Honeybee		Oral: LD_{50} > 293.0 µg/bee	

Test Material	Organism, Life Stage	Exposure Route (Duration)	Summary	Guideline #, MRID, Classification, Comments
JE874-224	Honeybee		Contact: LD_{50} > 200 µg/bee	

Several qualitative Tier II studies are available where honey bee colonies were exposed to indoxacarb. Effects observed in these studies and comments regarding specific limitations for quantitative use for estimating risks are summarized in **Table 47**. There are several common limitations across the colony feeding studies: single test concentration, dose tested below estimated dose for pollen and nectar for current labled rates, swarming and/or food stress, and low replication. Studies were conducted on bees fed a sucrose feeding solution at 100 - 155 µg a.i./kg-sucrose/day. One study (MRID 49544303) showed effects at those dose rates, while the other studies suggest no significant effects on larvae or adults. The available semi-field tunnel studies also have several common limitations: test concentration below labeled field rates, pre-application and tunnel effects, swarming, and low replication. Tested application rates from 0.0335 to 0.669 lbs a.i./A showed effects based on mortality and brood development, however in another study at 0.0446 lbs a.i./A effects were considered not significant. An additional subset of honeybee Tier II studies (MRIDs, 47327801, 47327802, 47327803, 49366001, 49366005, 49366007, 4936008, 49511504, 49566201) are currently under review.

No full field toxicity studies involving honey bee colonies exposed to indoxacarb are available.

Table 47. Summary of Tier II Honeybee Studies

Test Material	Organism	Study Type	Summary	MRID/ Study/Classification/Comments
Current Technical Formulation (Refined S-Isomer)				
DPX-JW062 Technical	Honeybee	Colony Feeding Study	Significant effects to mortality and brood development were observed in colonies treated with NOAEL < 100 µg a.i./kg-sucrose/day	Non-Guideline MRID 49544303 Supplemental Qualitative; uncertainties related to low replication, a single test concentration and effects observed in treatment group. Test concentration is below the estimated exposure through pollen and nectar using BEEREX and the maximum application rate.

DPX-JW062 Technical	Honeybee	Colony Feeding Study	No effects to mortality or brood development were observed in colonies treated with 100 µg a.i./kg-sucrose/day	Non-Guideline MRID 49782301 Supplemental Qualitative; Low replication, single dose administration, test concentration is below the estimated exposure through pollen and nectar using BEEREX and the maximum application rate
Product Formulations (Based on Old Technical)				
DPX-MP062 30WG	Honeybee	Colony Feeding Study	No effects to mortality or brood development were observed in colonies treated with 0.158 mg a.i./kg-sucrose/day (~0.117 mg KN128/kg)	Non-Guideline MRID 49859901 Supplemental Qualitative; uncertainties related to reported limitation of food resources for several test colonies, swarming and replication
Product Formulations (Based on New Technical)				
KN-128 150EC	Honeybee	Semi Field Tunnel Study	Evening and During Flight Application: No effects to mortality or brood development were observed in colonies treated with NOAEL = 0.0335 lbs a.i./A of indoxacarb (DPX-KN128) 150 G/L EC	Non-Guideline MRID 49544302 Supplemental Qualitative; Uncertainties related to pre-application effects that were most likely a result of the tunnels. Conducted at application rate that is lower than the lowest U.S. application rate.
KN-128 150EC	Honeybee	Colony Feeding Study	No effects to mortality or brood development were observed in colonies treated with NOAEL = 100 µg a.i./kg-sucrose/day.	Non-Guideline MRID 49544304 Supplemental Qualitative; uncertainties related to low replication and a single tested concentration.
KN-128 150EC	Honeybee	Semi Field Tunnel Study	Significant effects to colonies were observed in colonies treated with 0.0335 lbs a.i./A of indoxacarb (DPX-KN128) 150 g/L EC	Non-Guideline MRID 49544305 Supplemental Qualitative; uncertainties related to low replication, a single tested concentration, low application rate and pre-application effects.

KN-128 150EC	Honeybee	Semi Field Tunnel Study	Significant effects to colonies were observed in colonies treated with 0.0446 lbs a.i./A of indoxacarb (DPX-KN128) 150 g/L EC	Guideline MRID 49544306 Supplemental Qualitative; uncertainties related to low replication, a single tested concentration, low application rate and pre-application effects.
KN-128 30WG	Honeybee	Semi Field Tunnel Study	NOAEL=Not Determined. The tested concentration (0.0446 lbs a.i./A) does not test high enough to represent the highest exposure potential based on maximum label rates. No statistically or biologically significant effects were observed	Non-Guideline MRID 49321501 Supplemental Qualitative; Uncertainties related to low replication, low application rate, and a single tested concentration
KN-128 30WG	Honeybee	Semi Field Tunnel Study	Effects to mortality and brood development were observed in colonies treated with 0.0669 lbs a.i./A of indoxacarb a.s.	Non-Guideline MRID 49321502 Supplemental Qualitative; Uncertainties related to low replication, single dose tested, and pre-application effects

A honeybee toxicity of residues on foliage study was submitted for use of an old product formulation (formulated from old technical) on alfalfa (**Table 48**). The results indicate that significant mortality had occurred after exposure to plant residues 3 to 24 hours after application for application rates similar to those currently labled on alfalfa.

Table 48. Summary of available Residual Toxicity on Foliage Studies

Test Material	Organism	Study Type	Summary	MRID/ Study/Classification/Comments
DPX-MP062 30WG	Honeybee	Honeybee toxicity of residues on foliage	DPX-MP062 at a rate of 0.11866 lbs a.i/A caused significantly greater mortality upon exposure of bees for 24 hours to 3-hour aged alfalfa residues. DPX-MP062 at a rate of 0.149 lbs a.i./A caused significantly greater mortality upon exposure of	Non-Guideline MRID 44477236 Acceptable; The amount of test material applied to the alfalfa was three times greater than required.

			bees for 24 hours to all three groups of aged alfalfa residues (ie 3-,8-, and 24-hours).	

Several Tier I toxicity studies evaluating the effects of indoxacarb on bumble bees were submitted. The most sensitive contact based LD_{50} = 0.23 ug a.i./bee and on an oral exposure basis the LC_{50} = 0.065 ug a.i./bee (**Table 49**). These studies suggest similar toxicity to bumble bees as with honeybees (contact= 0.068 ug a.i./bee, oral = 0.204 ug a.i./L). This assessment relies upon the honeybee toxicity and exposure estimation of risk as a surrogate for bumble bees.

Table 49. Summary of bumble bee Tier I ecological effects data

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
Current Technical Formulation (Refined S-Isomer)			
DPX-JW062 Technical	Bumblebee	**<u>Oral:</u> LC_{50}=0.065 µg a.i./bee** **<u>Contact:</u> LD_{50}=0.23 µg a.i./bee**	Guideline 850.3020 MRID 49511501 Supplemental Quantitative (Highly toxic); Conducted with *Bombus*, a non-guideline species.
Product Formulations (Based on Old Technical)			
DPX-MP062 150SC	Bumblebee	<u>Oral:</u> LC_{50}=0.110 µg a.i./bee <u>Contact:</u> LD_{50}=0.31 µg a.i./bee	Guideline 850.3020 MRID 4951502 Supplemental Quantitative (Highly toxic); Used non-guideline test species, % active ingredient not specified, negative control not conducted according to guideline recommendations
DPX-MP062 30WG	Bumblebee	<u>Oral:</u> LC50=0.0912 ug a.i./bee <u>Contact:</u> LD50=0.64 ug a.i./bee	Guideline 850.3020 MRID 49544307 Supplemental Quantitative (Highly toxic); Conducted with *Bombus*, a non-guideline species.
DPX-MP062 30WG	*Bumblebee*	<u>Oral:</u> LC_{50}=0.0842 µg a.i./bee <u>Contact:</u> LC_{50}=0.56 µg a.i./bee	Guideline 850.3020 MRID 49544308 Supplemental Quantitative;

Test Material	Organism	Summary	Guideline #, MRID, Classification, Comments
			Conducted with *Bombus*, a non-guideline species.

Additional Terrestrial Invertebrates

A suite of terrestrial invertebrate studies (earthworms, predatory mite, lacewing, staphylinid beetle, parasitic wasp, collembolan) were screened (MRIDs 47695901, 49544316, 45779201, 49566207, 49544315, 49544319, 49544312, 49544321, 49544314, 49544313, 4574402, 45779201, 49544320, 49544317, 49544318, 44477237-42, and 45744201). These studies did not provide more sensitive endpoints and were not subjected to review or further evaluation.

5.3 ECOTOX Search and Review of Open Literature

An open literature review was conducted using the ECOTOX database (1990-2016, USEPA 2009). There were no additional terrestrial or aquatic studies that show greater toxicity than available studies; therefore, the registrant submitted data represent the most sensitive apical endpoints for evaluating risk.

5.4 Incident Information

A review on March 3, 2017 of the Incident Data System (IDS), which is maintained by the Agency's Office of Pesticide Programs, indicates a total of three reported ecological incidents associated with the use of Indoxacarb (**Table 50**). In addition to the incidents recorded in IDS, additional incidents are reported to the Agency in aggregated form. Pesticide registrants report certain types of incidents to the Agency as aggregate counts of incidents occurring per product per quarter. Ecological incidents reported in aggregate reports include those categorized as 'minor fish and wildlife' (W-B), 'minor plant' (P-B), and 'other non-target' (ONT) incidents. 'Other non-target' incidents include reports of adverse effects to insects and other terrestrial invertebrates. Since the most recent assessment and problem formulation where 1 ONT and 1 PB incidents were reported, 3 additional ONT and 1 additional WB incidents have been reported. These incidents are described in more detail in US EPA Document 2016, DP 428813. The number of actual incidents associated with indoxacarb may be higher than what is reported by the Agency. Incidents may go unreported since side effects may not be immediately apparent or readily attributed to the use of a chemical. Although incident reporting is required under FIFRA Section 6(a) (2), the absence of reports in EIIS does not indicate that the chemical has no effects on wildlife; rather, it is possible that incidents are unnoticed and unreported.

Table 50. Details of Incidents Associated with the Use of Indoxacarb form the Incident Data System

Incident # Date	Species	Use Site	State	Magnitude	Response	Route of Exposure	Certainty	Legality
I014139-007 5/24/2003	Apricot	Tomato	CA	$250,000	Plant Damage	Drift, Spray	Probable	Registered use
I016479-001 8/14/1999	Bee	Cotton	CA	164 Bee hives	Mortality	Treated directly	Possible	Registered use
I016138-001 10/11/2004	Cauliflower	Cauliflower	CA	70 Acres	Plant Damage	Treated Directly	Unlikely	Registered Use

5.5 Evaluation of mixtures

The Agency does not routinely include, in its risk assessments, an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator's tank. In the case of the product formulations of active ingredients (that is, a registered product containing more than one active ingredient), each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product containing more than one active ingredient, they may be used qualitatively or quantitatively in accordance with the Agency's Overview Document and the Services' Evaluation Memorandum (USEPA 2004; USFWS/NMFS/NOAA 2004).

6.0 Risk Estimation and Characterization

This preliminary assessment of indoxacarb was used to provide a metric for potential risks based on the RQ method, which is a comparison of exposure estimates to toxicity endpoints (*i.e.*, RQ = EEC/toxicity endpoint). The resulting RQs are compared to the Agency's risk levels of concern (LOC) criteria, which are the Agency's interpretive policy such that when acute or chronic risk LOCs are exceeded, the need for regulatory action may be considered. The acute LOC (0.5) is for non-listed terrestrial birds, mammals and aquatic animals, and the acute LOC (0.5) is for non-listed terrestrial invertebrates. The acute LOC (0.1) is for listed terrestrial birds and mammals, and LOC (0.05) is for listed aquatic animals and terrestrial invertebrates. The chronic LOC (1) is the same for all listed and non-listed terrestrial birds, mammals and invertebrates, and aquatic animals. For terrestrial and aquatic plants, the LOC (1) is same for both non-listed species (based on the estimation of EEC/EC_{25}) and listed species (based on estimation of EEC/EC_{05} or NOAEL). For honeybees, the acute LOC = 0.4 and the chronic LOC = 1.0.

6.1 Risk Concerns to Aquatic Organisms

As discussed in the exposure modeling section above, this assessment relied upon a Toxic Equivalency (TEQ) approach for estimating risk to aquatic taxa. For all comparisons, the cumulative concentration of indoxacarb and the degradates JT333 and MP819 were adjusted to indoxacarb equivalents based on the ratio of the toxicities for each degradate and taxon (**Table 51**). The most sensitive toxicity endpoints for indoxacarb are listed in **Table 8** were used to calculate the RQs based on the TEQ based EEC (**Table 51**). Agricultural and non-agricultural TEQ EECs were generally similar and result in similar risk profiles, for this reason the risks are discussed broadly in the following taxon based discussions.

Table 51. Water column TEQ EECs and RQs for freshwater and estuarine/marine fish and invertebrates (highlighted cells indicate exceedances; non-listed LOC (bold) and listed LOC (italics) exceedance).

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
Alfalfa	0.11 lbs a.i./A x 4 Aerial 3-day interval	CA Alfalfa	0.0020	<0.01	0.0010	<0.01	0.0021	<0.01	0.0008	0.05	0.0021	<0.01	0.0014	0.02	0.0020	0.04	0.0013	0.07
		IL Alfalfa	0.0028	<0.01	0.0026	0.04	0.0042	0.01	0.0018	0.11	0.0044	<0.01	0.0024	0.59	0.0028	*0.05*	0.0019	0.10
		MN Alfalfa	0.0019	<0.01	0.0008	0.01	0.0020	<0.01	0.0007	0.04	0.0020	<0.01	0.0012	0.30	0.0019	0.04	0.0012	0.06
		NC Alfalfa	0.0028	<0.01	0.0023	0.03	0.0038	0.01	0.0017	0.10	0.0040	<0.01	0.0024	0.59	0.0029	*0.05*	0.0019	<0.01
		TX Alfalfa	0.0036	0.01	0.0021	0.03	0.0048	0.01	0.0016	0.09	0.0051	<0.01	0.0027	0.65	0.0036	*0.07*	0.0022	0.12
	0.11 lbs a.i./A x 4 Chemigation 3-day interval	CA Alfalfa	0.0006	<0.01	0.0005	<0.01	0.0009	<0.01	0.0003	0.02	0.0010	<0.01	0.0004	0.11	0.0005	<0.01	0.0003	0.02
		IL Alfalfa	0.0022	<0.01	0.0023	0.03	0.0032	<0.01	0.0014	0.08	0.0034	<0.01	0.0019	0.47	0.0022	0.04	0.0013	0.07
		MN Alfalfa	0.0004	<0.01	0.0002	<0.01	0.0006	<0.01	0.0002	0.01	0.0007	<0.01	0.0003	0.07	0.0005	<0.01	0.0002	0.01
		NC Alfalfa	0.0022	<0.01	0.0019	0.03	0.0033	<0.01	0.0012	0.07	0.0036	<0.01	0.0019	0.47	0.0022	0.04	0.0014	0.08
		TX Alfalfa	0.0029	<0.01	0.0017	0.03	0.0041	0.01	0.0012	0.07	0.0044	<0.01	0.0020	0.48	0.0029	*0.05*	0.0015	0.08
	0.11 lbs a.i./A x 4 Ground 3-day interval	CA Alfalfa	0.0010	<0.01	0.0007	0.01	0.0015	<0.01	0.0005	0.03	0.0015	<0.01	0.0008	0.20	0.0010	0.02	0.0007	0.04
		IL Alfalfa	0.0024	<0.01	0.0025	0.04	0.0034	<0.01	0.0016	0.09	0.0037	<0.01	0.0021	0.52	0.0024	0.04	0.0015	0.08
		MN Alfalfa	0.0010	<0.01	0.0005	<0.01	0.0011	<0.01	0.0004	0.03	0.0011	<0.01	0.0007	0.17	0.0010	0.02	0.0007	0.04
		NC Alfalfa	0.0025	<0.01	0.0021	0.03	0.0036	<0.01	0.0015	0.09	0.0039	<0.01	0.0022	0.54	0.0025	*0.05*	0.0017	0.09
		TX Alfalfa	0.0033	0.01	0.0019	0.03	0.0045	0.01	0.0014	0.08	0.0048	<0.01	0.0023	0.55	0.0033	*0.06*	0.0018	0.10
Bean	0.11 lbs a.i./A x 4 Aerial 3-day interval	MI Beans	0.0040	0.01	0.0041	0.06	0.0061	0.02	0.0025	0.15	0.0063	0.01	0.0034	0.83	0.0037	*0.07*	0.0024	0.13
		OR Snap Beans	0.0027	<0.01	0.0036	0.05	0.0034	<0.01	0.0023	0.14	0.0035	<0.01	0.0027	0.66	0.0026	*0.05*	0.0020	0.11
		MI Beans	0.0036	0.01	0.0038	0.06	0.0059	0.02	0.0023	0.14	0.0061	0.01	0.0030	0.72	0.0032	*0.06*	0.0020	0.11

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	0.11 lbs a.i./A x 4 Ground 3-day interval	OR Snap Beans	0.0022	<0.01	0.0035	0.05	0.0033	<0.01	0.0022	0.13	0.0034	<0.01	0.0025	0.60	0.0020	0.04	0.0017	0.09
Beet	0.11 lbs a.i./A x 4 Aerial 3-day interval	MN Sugarbeet	0.0024	<0.01	0.0025	0.04	0.0030	<0.01	0.0017	0.10	0.0031	<0.01	0.0023	0.55	0.0024	0.04	0.0018	0.10
	0.11 lbs a.i./A x 4 Ground 3-day interval	MN Sugarbeet	0.0017	<0.01	0.0022	0.03	0.0026	<0.01	0.0014	0.08	0.0026	<0.01	0.0017	0.42	0.0015	0.03	0.0012	0.07
Cucurbit	0.11 lbs a.i./A x 4 Aerial 3-day interval	FL Cucurbit	0.0038	0.01	0.0029	0.04	0.0050	0.01	0.0019	0.11	0.0047	<0.01	0.0023	0.55	0.0032	*0.06*	0.0018	0.10
	0.11 lbs a.i./A x 4 Ground 3-day interval	FL Cucurbit	0.0035	0.01	0.0028	0.04	0.0049	0.01	0.0018	0.11	0.0044	<0.01	0.0021	0.51	0.0027	*0.05*	0.0016	0.08
Grape, Strawberry	0.11 lbs a.i./A x 4 Aerial 3-day interval	CA Grape	0.0019	<0.01	0.0008	0.01	0.0020	<0.01	0.0007	0.04	0.0020	<0.01	0.0012	0.29	0.0019	0.04	0.0011	0.06
		NY Grape	0.0147	*0.05*	0.0244	0.36	0.0282	*0.08*	0.0136	0.81	0.0284	*0.05*	0.0159	**3.87**	0.0115	*0.21*	0.0088	0.48
		FL Strawberry	0.0033	0.01	0.0018	0.03	0.0041	0.01	0.0013	0.08	0.0043	<0.01	0.0020	0.50	0.0033	*0.06*	0.0018	0.10
	0.11 lbs a.i./A x 4	CA Grape	0.0010	<0.01	0.0005	<0.01	0.0010	<0.01	0.0004	0.02	0.0010	<0.01	0.0006	0.16	0.0010	0.02	0.0006	0.03
		NY Grape	0.0146	*0.05*	0.0242	0.36	0.0281	*0.08*	0.0134	0.79	0.0284	*0.05*	0.0157	**3.82**	0.0114	*0.21*	0.0086	0.47

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	Ground 3-day interval	FL Strawberry	0.0028	<0.01	0.0017	0.03	0.0040	0.01	0.0012	0.07	0.0042	<0.01	0.0018	0.44	0.0028	*0.05*	0.0014	0.08
Leafy Greens/Vegs	0.11 lbs a.i./A x 4 Aerial 3-day interval	CA Lettuce	0.0032	0.01	0.0024	0.04	0.0045	0.01	0.0017	0.10	0.0046	<0.01	0.0023	0.57	0.0029	*0.05*	0.0019	0.10
	0.11 lbs a.i./A x 4 Ground 3-day interval	CA Lettuce	0.0027	<0.01	0.0021	0.03	0.0042	0.01	0.0014	0.08	0.0043	<0.01	0.0019	0.46	0.0024	0.04	0.0014	0.08
	0.11 lbs a.i./A x 4 Aerial 3-day interval 4 Seasons	CA Lettuce	0.0089	0.03	0.0075	0.11	0.0110	0.03	0.0052	0.31	0.0111	0.02	0.0065	**1.58**	0.0085	*0.16*	0.0051	0.28
	0.11 lbs a.i./A x 4 Ground 3-day interval 4 Seasons	CA Lettuce	0.0089	0.03	0.0073	0.11	0.0110	0.03	0.0050	0.29	0.0111	0.02	0.0064	**1.56**	0.0085	*0.16*	0.0050	0.27
	0.065 lbs a.i./A x 4 Aerial 3-day interval	CA Lettuce	0.0019	<0.01	0.0014	0.02	0.0027	<0.01	0.0010	0.06	0.0027	<0.01	0.0014	0.33	0.0017	0.03	0.0011	0.06
	0.065 lbs a.i./A x 4 Ground 3-day interval	CA Lettuce	0.0016	<0.01	0.0012	0.02	0.0025	<0.01	0.0008	0.05	0.0025	<0.01	0.0011	0.27	0.0014	0.03	0.0008	0.05

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
Peanut	0.11 lbs a.i./A x 4 Aerial 3-day interval	NC Peanut	0.0080	0.03	0.0095	0.14	0.0141	0.04	0.0054	0.32	0.0142	0.02	0.0069	**1.67**	0.0065	*0.12*	0.0043	0.23
	0.11 lbs a.i./A x 4 Chemigation 3-day interval	NC Peanut	0.0066	0.02	0.0094	0.14	0.0127	0.03	0.0052	0.31	0.0127	0.02	0.0060	**1.45**	0.0053	*0.10*	0.0035	0.19
	0.11 lbs a.i./A x 4 Ground 3-day interval	NC Peanut	0.0073	0.03	0.0094	0.14	0.0134	0.04	0.0052	0.31	0.0134	0.02	0.0064	**1.57**	0.0057	*0.11*	0.0040	0.22
Pome Fruits	0.11 lbs a.i./A x 4 Aerial 3-day interval	NC Apple	0.0052	0.02	0.0063	0.09	0.0090	0.02	0.0039	0.23	0.0092	0.02	0.0053	**1.29**	0.0045	*0.08*	0.0034	0.18
		OR Apple	0.0021	<0.01	0.0011	0.02	0.0022	<0.01	0.0009	0.05	0.0022	<0.01	0.0014	0.34	0.0021	0.04	0.0013	0.07
		PA Apple	0.0065	0.02	0.0072	0.11	0.0113	0.03	0.0043	0.25	0.0113	0.02	0.0056	**1.35**	0.0054	*0.10*	0.0036	0.20
	0.11 lbs a.i./A x 4 Ground 3-day interval	NC Apple	0.0051	0.02	0.0062	0.09	0.0089	0.02	0.0037	0.22	0.0091	0.02	0.0052	**1.26**	0.0044	*0.08*	0.0033	0.18
		OR Apple	0.0011	<0.01	0.0008	0.01	0.0012	<0.01	0.0006	0.03	0.0013	<0.01	0.0009	0.21	0.0011	0.02	0.0008	0.04
		PA Apple	0.0060	0.02	0.0069	0.10	0.0108	0.03	0.0040	0.24	0.0108	0.02	0.0051	**1.24**	0.0049	*0.09*	0.0031	0.17
Root and Tuber Vegs	0.11 lbs a.i./A x 4 Aerial 3-day interval	ID Potato	0.0025	<0.01	0.0031	0.05	0.0032	<0.01	0.0020	0.12	0.0034	<0.01	0.0027	0.65	0.0026	*0.05*	0.0020	0.11
		ME Potato	0.0096	0.03	0.0186	0.28	0.0178	*0.05*	0.0103	0.61	0.0179	0.03	0.0121	**2.94**	0.0081	*0.15*	0.0069	0.38
		NC Sweet Potato	0.0106	0.04	0.0155	0.23	0.0194	*0.05*	0.0088	0.52	0.0195	0.03	0.0109	**2.64**	0.0084	*0.16*	0.0064	0.35
	0.11 lbs a.i./A x 4	ID Potato	0.0009	<0.01	0.0026	0.04	0.0017	<0.01	0.0015	0.09	0.0019	<0.01	0.0018	0.43	0.0009	0.02	0.0011	0.06
		ME Potato	0.0092	0.03	0.0181	0.27	0.0173	*0.05*	0.0099	0.59	0.0178	0.03	0.0116	**2.81**	0.0073	*0.13*	0.0064	0.35

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	Chemigation 3-day interval	NC Sweet Potato	0.0095	0.03	0.0152	0.22	0.0184	*0.05*	0.0084	0.50	0.0185	0.03	0.0102	**2.48**	0.0076	*0.14*	0.0056	0.31
	0.11 lbs a.i./A x 4 Ground 3-day interval	ID Potato	0.0016	<0.01	0.0028	0.04	0.0024	<0.01	0.0018	0.10	0.0025	<0.01	0.0022	0.52	0.0016	0.03	0.0015	0.08
		ME Potato	0.0096	0.03	0.0183	0.27	0.0175	*0.05*	0.0101	0.60	0.0179	0.03	0.0118	**2.86**	0.0077	*0.14*	0.0067	0.36
		NC Sweet Potato	0.0101	0.03	0.0153	0.23	0.0189	*0.05*	0.0086	0.51	0.0190	0.03	0.0105	**2.55**	0.0079	*0.15*	0.0060	0.33
Stone Fruit	0.11 lbs a.i./A x 4 Aerial 3-day interval	MI Cherry	0.0086	0.03	0.0135	0.20	0.0152	0.04	0.0076	0.45	0.0152	0.03	0.0088	**2.14**	0.0068	*0.13*	0.0050	0.27
		GA Peach	0.0034	0.01	0.0022	0.03	0.0054	0.01	0.0015	0.09	0.0055	<0.01	0.0024	0.57	0.0030	*0.06*	0.0018	0.10
		CA Fruit	0.0019	<0.01	0.0008	0.01	0.0020	<0.01	0.0007	0.04	0.0020	<0.01	0.0013	0.31	0.0020	0.04	0.0012	0.07
	0.11 lbs a.i./A x 4 Ground 3-day interval	MI Cherry	0.0077	0.03	0.0134	0.20	0.0148	0.04	0.0075	0.44	0.0150	0.03	0.0087	**2.12**	0.0060	*0.11*	0.0049	0.26
		GA Peach	0.0032	0.01	0.0020	0.03	0.0054	0.01	0.0013	0.08	0.0054	<0.01	0.0019	0.47	0.0028	*0.05*	0.0014	0.07
		CA Fruit	0.0010	<0.01	0.0006	<0.01	0.0011	<0.01	0.0004	0.03	0.0011	<0.01	0.0007	0.18	0.0010	0.02	0.0007	0.04
Brassica	0.065 lbs a.i./A x 4 Aerial 3-day interval	CA Cole Crop	0.0024	<0.01	0.0028	0.04	0.0038	0.01	0.0018	0.11	0.0039	<0.01	0.0022	0.53	0.0022	0.04	0.0016	0.08
	0.065 lbs a.i./A x 4 Ground 3-day interval	CA Cole Crop	0.0021	<0.01	0.0027	0.04	0.0033	<0.01	0.0016	0.10	0.0035	<0.01	0.0021	0.50	0.0019	0.03	0.0014	0.07
Mint	0.065 lbs a.i./A x 4 Aerial 3-day interval	OR Mint	0.0012	<0.01	0.0005	<0.01	0.0012	<0.01	0.0005	0.03	0.0012	<0.01	0.0008	0.19	0.0012	0.02	0.0007	0.04

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	0.065 lbs a.i./A x 4 Chemigation 3-day interval	OR Mint	0.0004	<0.01	0.0003	<0.01	0.0005	<0.01	0.0002	0.01	0.0005	<0.01	0.0002	0.06	0.0004	<0.01	0.0002	0.01
	0.065 lbs a.i./A x 4 Ground 3-day interval	OR Mint	0.0006	<0.01	0.0004	<0.01	0.0007	<0.01	0.0003	0.02	0.0007	<0.01	0.0005	0.11	0.0006	0.01	0.0004	0.02
Fruiting Vegetables	0.065 lbs a.i./A x 4 Aerial 3-day interval	FL Pepper	0.0034	0.01	0.0023	0.03	0.0051	0.01	0.0015	0.09	0.0054	<0.01	0.0025	0.61	0.0033	*0.06*	0.0019	0.10
		CA Tomato	0.0011	<0.01	0.0005	<0.01	0.0012	<0.01	0.0004	0.03	0.0012	<0.01	0.0007	0.18	0.0011	0.02	0.0007	0.04
		FL Tomato	0.0024	<0.01	0.0021	0.03	0.0036	<0.01	0.0014	0.08	0.0038	<0.01	0.0019	0.47	0.0024	0.04	0.0015	0.08
		PA Tomato	0.0071	0.02	0.0078	0.12	0.0131	0.04	0.0044	0.26	0.0131	0.02	0.0060	**1.46**	0.0055	*0.10*	0.0035	0.19
	0.065 lbs a.i./A x 4 Ground 3-day interval	FL Pepper	0.0034	0.01	0.0023	0.03	0.0051	0.01	0.0015	0.09	0.0054	<0.01	0.0025	0.60	0.0033	*0.06*	0.0019	0.10
		CA Tomato	0.0006	<0.01	0.0003	<0.01	0.0008	<0.01	0.0003	0.02	0.0008	<0.01	0.0004	0.11	0.0006	0.01	0.0004	0.02
		FL Tomato	0.0023	<0.01	0.0020	0.03	0.0036	<0.01	0.0014	0.08	0.0038	<0.01	0.0019	0.47	0.0022	0.04	0.0015	0.08
		PA Tomato	0.0068	0.02	0.0077	0.11	0.0128	0.03	0.0043	0.25	0.0128	0.02	0.0059	**1.44**	0.0052	*0.10*	0.0034	0.18
Sweet Corn	0.065 lbs a.i./A x 4 Aerial 3-day interval	FL Sweet Corn	0.0022	<0.01	0.0017	0.02	0.0031	<0.01	0.0011	0.07	0.0032	<0.01	0.0015	0.36	0.0023	0.04	0.0012	0.07
		OR Sweet Corn	0.0016	<0.01	0.0022	0.03	0.0022	<0.01	0.0014	0.08	0.0022	<0.01	0.0017	0.41	0.0016	0.03	0.0012	0.07
	0.065 lbs a.i./A x 4 Chemigation 3-day interval	FL Sweet Corn	0.0020	<0.01	0.0015	0.02	0.0028	<0.01	0.0010	0.06	0.0030	<0.01	0.0013	0.31	0.0019	0.03	0.0009	0.05
		OR Sweet Corn	0.0014	<0.01	0.0021	0.03	0.0020	<0.01	0.0013	0.08	0.0021	<0.01	0.0015	0.35	0.0012	0.02	0.0009	0.05

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	0.065 lbs a.i./A x 4 Ground 3-day interval	FL Sweet Corn	0.0022	<0.01	0.0016	0.02	0.0030	<0.01	0.0011	0.06	0.0032	<0.01	0.0014	0.33	0.0022	0.04	0.0011	0.06
		OR Sweet Corn	0.0015	<0.01	0.0022	0.03	0.0022	<0.01	0.0014	0.08	0.0022	<0.01	0.0015	0.37	0.0013	0.02	0.0010	0.06
Cotton	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0021	<0.01	0.0027	0.04	0.0028	<0.01	0.0018	0.10	0.0030	<0.01	0.0023	0.56	0.0022	0.04	0.0017	0.09
		MS Cotton	0.0100	0.03	0.0135	0.20	0.0181	*0.05*	0.0079	0.46	0.0181	0.03	0.0100	**2.44**	0.0081	*0.15*	0.0060	0.32
		NC Cotton	0.0105	0.04	0.0171	0.25	0.0199	*0.05*	0.0097	0.58	0.0200	0.03	0.0115	**2.79**	0.0082	*0.15*	0.0066	0.36
	0.11 lbs a.i./A x 4 Chemigation 5-day interval	CA Cotton	0.0009	<0.01	0.0023	0.03	0.0016	<0.01	0.0013	0.08	0.0018	<0.01	0.0016	0.40	0.0009	0.02	0.0010	0.06
		MS Cotton	0.0090	0.03	0.0132	0.19	0.0171	*0.05*	0.0074	0.44	0.0171	0.03	0.0098	**2.39**	0.0079	*0.15*	0.0058	0.31
		NC Cotton	0.0099	0.03	0.0167	0.25	0.0193	*0.05*	0.0094	0.56	0.0194	0.03	0.0113	**2.74**	0.0076	*0.14*	0.0063	0.35
	0.11 lbs a.i./A x 4 Ground 5-day interval	CA Cotton	0.0014	<0.01	0.0025	0.02	0.0021	<0.01	0.0015	0.09	0.0023	<0.01	0.0019	0.03	0.0015	0.03	0.0013	0.07
		MS Cotton	0.0096	0.03	0.0133	0.20	0.0177	*0.05*	0.0077	0.45	0.0177	0.03	0.0100	**2.42**	0.0081	*0.15*	0.0059	0.32
		NC Cotton	0.0103	0.04	0.0170	0.25	0.0197	*0.05*	0.0096	0.57	0.0198	0.03	0.0114	**2.78**	0.0080	*0.15*	0.0066	0.36
Soybean	0.11 lbs a.i./A x 4 Aerial 5-day interval	MS Soybean	0.0068	0.02	0.0079	0.12	0.0122	0.03	0.0047	0.28	0.0123	0.02	0.0060	**1.45**	0.0055	*0.10*	0.0036	0.19
	0.11 lbs a.i./A x 4 Chemigation 5-day interval	MS Soybean	0.0063	0.02	0.0078	0.11	0.0116	0.03	0.0044	0.26	0.0118	0.02	0.0054	**1.32**	0.0050	*0.09*	0.0033	0.18
	0.11 lbs a.i./A x 4	MS Soybean	0.0066	0.02	0.0078	0.12	0.0120	0.03	0.0045	0.27	0.0121	0.02	0.0058	**1.41**	0.0053	*0.10*	0.0035	0.19

Crop	Application Rate, Number of Applications, Method, Interval, Number of Seasons	PWC Scenario	FW Fish Acute		FW Fish Chronic		E/M Fish Acute		E/M Fish Chronic		FW Invertebrate Acute		FW Invertebrate Chronic		E/M Invertebrate Acute		E/M Invertebrate Chronic	
			TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ	TEQ EEC	TEQ RQ
	Ground 5-day interval																	
Residential Perimeter	0.11 lbs a.i./A x 4 Perimeter Granule 3-day interval	Residential Perimeter	0.0008	<0.01	0.0008	0.01	0.0014	<0.01	0.0005	0.03	0.0016	<0.01	0.0008	0.20	0.0008	*0.02*	0.0005	0.03
	1.437 lbs a.i./A x 4 Perimeter Spray 3-day interval		0.0020	<0.01	0.0005	<0.01	0.0024	<0.01	0.0006	0.03	0.0051	<0.01	0.0021	0.51	0.0050	*0.09*	0.0021	0.11
Turf	0.44 lbs a.i./A Ground	FL Turf	0.0016	<0.01	0.0004	<0.01	0.0016	<0.01	0.0004	0.02	0.0016	<0.01	0.0006	0.15	0.0016	*0.03*	0.0006	0.03
		PA Turf	0.0018	<0.01	0.0012	0.02	0.0021	<0.01	0.0008	0.05	0.0022	<0.01	0.0013	0.31	0.0018	*0.03*	0.0010	0.06
	0.225 lbs a.i./A x 2 Ground 7-day interval	FL Turf	0.0011	<0.01	0.0004	<0.01	0.0011	<0.01	0.0004	0.02	0.0011	<0.01	0.0006	0.14	0.0011	*0.02*	0.0006	0.03
		PA Turf	0.0014	<0.01	0.0013	0.02	0.0018	<0.01	0.0009	0.05	0.0020	<0.01	0.0013	0.31	0.0015	*0.03*	0.0010	0.05
	0.0375 lbs a.i./A x 12 Ground 7-day interval	FL Turf	0.0007	<0.01	0.0004	<0.01	0.0009	<0.01	0.0003	0.02	0.0009	<0.01	0.0004	0.10	0.0007	*0.01*	0.0004	0.02
		PA Turf	0.0013	<0.01	0.0015	0.02	0.0020	<0.01	0.0009	0.06	0.0022	<0.01	0.0012	0.30	0.0014	*0.03*	0.0009	0.05

Fish

The TEQ EECs did not exceed the acute or chronic non-listed LOCs for fish. The acute listed species LOC (0.05) was reached for freshwater fish based on exposures estimated for ground and aerial applications to grapes or strawberries in the NY-Grape scenario (RQs 0.05). The NY Grape scenario and scenarios used for root and tuber crops, and cotton generated RQs above the acute listed estuarine marine fish LOC (RQs 0.08). While these exceedances have been identified here for fish, it is important to consider that for estuarine marine fish the available acute and chronic data for DPX-MP062 on sheepshead minnow were non-definitive. These estimated endpoints along with a non-definitive rainbow trout study with IN-JT333 were used in the estimation of the TEQ ratio (see **Error! Reference source not found.** and Table 7). This contributes to the uncertainty of the exposure/toxicity relationship which may overestimate the risks to estuarine marine fish.

Aquatic Invertebrates

Grape and strawberry use scenarios were found to meet the acute LOC for listed freshwater invertebrates (RQs 0.05). On a chronic exposure basis there was identified more substantial exceedances of the LOC across multiple crops following a single application season (including grape and strawberry, peanuts, pome fruits, root and tuber vegetables, stone fruits, fruiting vegetables, cotton, and soybean uses). Multiple seasons (up to 4 application seasons/year) were assessed using the leafy greens use scenario to represent all crops for multiple crop cycles on a given acre. The RQs were 3-4 times higher than the same scenario with only a single application season and exceed the chronic LOC for leafy vegetables (RQs 1.58 - 1.56). The RQs for acute risks to estuarine marine invertebrates exceed acute listed LOCs for alfalfa, beans, cucurbits, grapes, strawberries, leafy greens and vegetables, peanuts, root and tuber crops, stone fruits, fruiting vegetables, cotton, soybean and residential perimeter treatments (RQs 0.01-0.21). These exceedances are uncertain given that the data used to calculated the estimated toxicity ratio for the TEQ was based upon non-definitive endpoints, and therefore may overestimate the toxicity and RQs. There were no exceedances of the chronic LOC for estuarine marine invertebrates.

It should be noted that the TEQ ratios for acute (IN-JT333) and chronic (IN-MP819 estimate) risk to freshwater fish relied upon a non-definitive endpoint for IN-JT333 to Daphnia magna. This contributes to the uncertainty of the exposure/toxicity relationship which may overestimate the risks to freshwater and estuarine marine invertebrates in the water column.

Exposures to benthic invertebrates were estimated with several different crop scenarios (**Table 52**). These comparisons consider the exposure via sediment as well as concentration in pore water and the relative concentration of indoxacarb and its degradates of concern. However, the persistence and propensity of indoxacarb to bind to sediment increases the exposure to these sediment dwelling taxa. The chronic LOC was exceeded for all evaluated use scenarios (RQs 0.86-486). These exposures are considered highly probable due to the sediment sorbing expected given the physiochemical properties of indoxacarb and its degradates. There is also a potential that these estimates underestimate the risks because the available study is not reproduction study, and thus may not reflect more sensitive effects that may occur over a longer exposure period. Additionally, there is uncertainty regarding exposure and effects to estuarine marine sediment dwelling invertebrates because of the propensity of indoxacarb and its degradates to sorb to sediments and the lack of an estuarine/marine chronic sediment toxicity study.

Table 52. Sediment TEQ EECs and RQs for pore water and sediment freshwater sediment invertebrate toxicity endpoints (highlighted and bolded cells indicate chronic LOC exceedance)

Crop	Application Rate, Method, and Interval	PWC Scenario	Pore Water TEQ EEC mg a.i./L	Chronic Pore Water RQ	Sediment TEQ EEC mg a.i./kg	Chronic Sediment RQ
Cotton	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0005	0.86	0.0808	**83.71**
		MS Cotton	0.0015	**2.73**	0.2041	**211.53**
		NC Cotton	0.0018	**3.28**	0.2349	**243.43**
Leafy Vegetables	0.11 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0024	**4.47**	0.4688	**485.81**
	0.11 lbs a.i./A x 4 Aerial 3-day interval 1 season	CA Lettuce	0.0007	**1.35**	0.1404	**145.54**
Soybean	0.11 lbs a.i./A x 4 Aerial 5-day interval	MS Soybean	0.0011	**1.95**	0.1558	**161.45**

Uncertainties in the estimation of risk using the TEQ Approach

Several factors were considered prior to selecting the TEQ approach for this assessment. The first series of considerations were related to the modeling assumptions for application rates and timing of application and formation of degradates. Under conditions where the degradate formation occurs over an extended period of time, such that the peak formation occurs a long period after the application of parent, the expected resulting peak estimate for exposures in water would come much later that the arrival of the parent compound. With indoxacarb, the degradates IN-JT333 and IN-MP819 each reach their peak formation at 7 and 3 days respectively. Therefore, the expectation is that the arrival and peak of these two degradates would be at approximately the same or very similar timeframe as indoxacarb. In the figure below, the approximate 1:10 year (1963) chemograph displays the PWC estimated concentrations for indoxacarb, IN-JT333 and IN-MP819. As illustrated in the figure, the concentrations for the degradates are far lower than that of parent indoxacarb and the assumed model parameters have them forming a peak exposure at roughly the same day as parent indoxacarb. These lines of evidence provide justification for our assumption of a same day application (peak formation) as the parent (**Figure 3**).

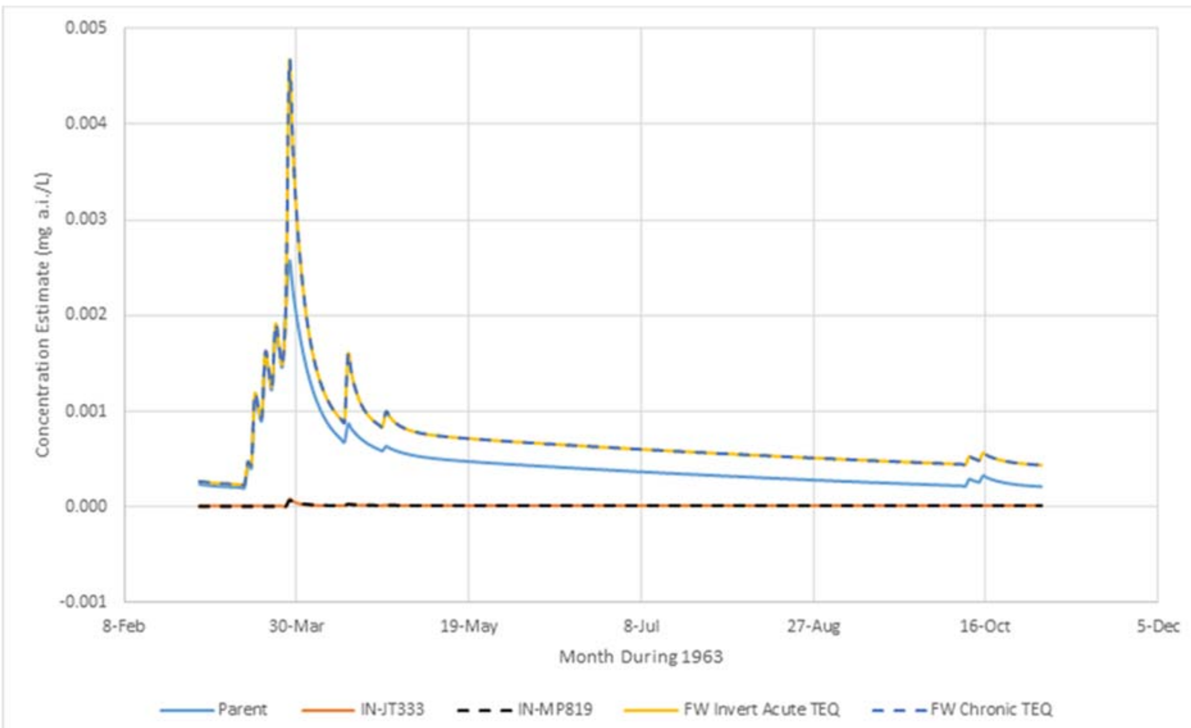

Figure 3. PWC estimated exposure chemograph for 1963. Curves represent the distribution of EECs for parent indoxacarb (blue), IN-JT333 (orange) and IN-MP819 (grey), as well as the TEQ adjusted parent EECs for acute and chronic freshwater invertebrates (yellow and blue respectively). Model Scenario: 0.11 lbs/A, 4 aerial applications, 3-day interval, CA Lettuce Scenario and a single season.

Another assumption is that the maximum formation of the degradates is captured in the available environmental fate studies. Since this is used as the application rate for each of the degradates, there is a potential that the EECs do not capture the highest potential EECs for the degradates. However, the available data limits the modeling approaches that are available. One comparison would be to assume that exposures are cumulative and use the most sensitive endpoint across the parent and two degradates, which is similar to a TTR approach because in a TTR approach modeling exercise the fate characteristics of indoxacarb are the most conservative and would be used. **Table 53 and 54** illustrate how the risk profile for fish and water column invertebrates would be affected if considering 1) parent only and its toxicity data, 2) a TTR approach against the most sensitive endpoints across all chemicals, 3 & 4) the two modeled degradates against their own toxicity data, and lastly the comparison to the TEQ based approach used in this assessment. As denoted by the bolded values in the table, the risks estimated for each approach are similarly predicting few LOC exceedances, with the exception of the TTR approach. However, we believe that the TTR approach is unreasonable given the relatively low rate of formation of the degradates in the available degradation studies and the highly differential toxicity of the degradates to the parent.

Table 53. Comparison of EEC estimation methods and resulting single season RQs (bold exceeds non-listed species LOC). EECs based on 4 aerial applications at 0.11 lbs/A, with a 3-day interval for the CA Lettuce Scenario.

Taxon and Duration of Exposure	Parent Only	Estimated TTR vs Most Sensitive Toxicity Endpoint[a]	JT333	MP819 RQs	TEQ
Acute FW Fish	0.01	0.09	0.00	0.00	0.01
Chronic FW Fish	0.01	0.74	0.03	0.00	0.04
Acute EM Fish	0.01	0.16	0.01	0.00	0.01
Chronic EM Fish	0.06	**1.56**	0.05	0.00	0.10
Acute FW Invert	0.00	0.02	0.00	0.00	<0.01
Chronic FW Invert	0.23	**4.67**	0.16	0.08	0.57
Acute EM Invert	0.04	0.04	0.00	0.02	0.05
Chronic EM Invert	0.08	0.74	0.01	0.02	0.10

[a] TTR used here refers to the parent only EECs estimated from PWC.

Table 54. Multiple Season RQs (bold exceeds non-listed species LOC) based on several assumptions of modeled EECs and toxicity. EECs based on assumptions for 0.11 lbs/A, 4 aerial applications, 3 day interval, CA Lettuce Scenario and 4 seasons.

Taxon and Duration of Exposure	**Parent Only**	**Estimated TTR vs Most Sensitive Toxicity Endpoint[a]**	**JT333**	**MP819 RQs**	**TEQ**
Acute FW Fish	0.02	0.30	0.01	0.00	0.03
Chronic FW Fish	0.04	**2.24**	0.09	0.00	0.11
Acute EM Fish	0.02	**0.51**	0.01	0.00	0.03
Chronic EM Fish	0.17	**4.71**	0.19	0.01	0.31
Acute FW Invert	0.01	0.06	0.00	0.00	0.02
Chronic FW Invert	0.69	**14.14**	0.56	0.27	**1.58**
Acute EM Invert	0.13	0.13	0.00	0.03	0.16
Chronic EM Invert	0.20	**1.90**	0.03	0.07	0.28

[a] TTR used here refers to the parent only EECs estimated from PWC.

Lastly, in the estimation of the TEQ toxicity ratios, a combination of data based on the old technical and new technical formulations was used to calculate several of the ratios. Based on the available technical formulation acute toxicity data for fish and estuarine marine invertebrates the two technical formulations have similar toxicity. The new formulation is approximately 2x more toxic than the old, which appears to be similar to background variablity within the measured tests. Therefore, there is low likelihood of a big influence on the estimated ratio or the resulting TEQ based RQ. Based on the available technical formulation for chronic toxicity data for fish and freshwater invertebrates, the new technical is similarly toxic for fish, however the endpoint for freshwater invertebrates is 18 times more toxic than the endpoint estimated from exposure to the old technical. This may be partly explained by the selected dose spacing in the studies, however the LOAEC for the new technical is below the NOAEC for the old technical. Thus, the combination of these two technical formulation endpoints for the calculation of the ratios may impose a greater differential toxicity and thus drive up the ratio and resulting TEQ based RQ. Because of these complications, several iterations of alternative ratio calculations (**Table 55**) were conducted to evaluate the impact on the largest TEQ RQs [Leafy Greens (4 seasons) and Grapes (single season) at 0.11 lbs a.i./A], to aid in the illustration of the uncertainty imposed on the estimates by relying on the approach taken in the assessment. For freshwater fish the adjusted ratio would be an increase, however this increased ratio does not result in exceedances of the chronic fish LOC. Likewise the adjusted ratios for estuarine marine fish based on either the Mysid data or the Daphnid data do not result in LOC exceedances. The largest changes in ratios were observed for the two degradates for freshwater invertebrates. These decreases in the ratios result in reduced RQs such that for the Leafy Greens at 0.11 lbs a.i./A and 4 seasons, the chronic RQ changes from 1.58 to 0.92, and for Grape at 0.11 the chronic RQ changes from 3.87 to 0.74. Therefore, the ratios used in the full TEQ RQ analysis (Table 55) may over estimate risks to freshwater invertebrates in the water column.

Table 55. Alternative toxicity ratios based on other available lines of evidence.

Modified Ratio	**Ratio used in the full TEQ RQ analysis (**Error! Reference source not found.**)**	**Ratio Estimated using Only New Technical Data**	**Ratio Estimated Using Only Old Technical Mysid**	**Ratio Estimated Using Only Old Technical Daphnid**
IN-MP819 Chronic FW Fish	0.75	0.90	NA[a]	NA[a]
IN-JT333 Chronic FW Invertebrate	18.3	NA[a]	0.4	1.0
IN-MP819 Chronic FW Invertebrate	8.84	NA[a]	0.18	0.48
IN-JT333 Chronic EM Invertebrate	4.70	NA[a]	0.70	1.89

[a]NA= Not applicable due to lack of data or inappropriate comparison

Aquatic plants

For aquatic plants, the definitive EC_{50} for *Skeletonema* and observed NOAEC values are more than 10X lower than the peak EECs. Therefore, risk of exceeding the aquatic plant LOCs is low.

6.2 Risk Concerns to Birds and Mammals

On-field risks for birds and mammals were first evaluated for a single season. Risk quotients exceeded both the listed and non-listed LOCs for several dietary groups and size classes for both birds and mammals at the minimum and maximum agricultural and non-agricultural application rates for multiple within season applications. A single application of indoxacarbof either 0.06525 or 0.1125 lbs a.i./A showed lower risk, but there were still exceedances of LOCs for birds and mammals.

These on-field modeled scenarios consider only one seasonal application period. However, indoxacarb can be applied for multiple seasons (as addressed in the aquatic assessment) for certain crops (**see Use Section**). Thus, the areas off the field that receive spray drift must be evaluated for LOC exceedences due to multiple applications and crop cycles.

The technical formulation of indoxacarb has changed over time from the original 75:25 percent mixture of *S* and *R* enantiomers to an enriched technical containing 95% of the *S*-enantiomer. The *R*-enantiomer has been considered less toxic in the past, but as for aquatics, the *S*-enantiomer has been considered the active ingredient. This assessment has based the toxicity in terms of the *S*-enantiomer. For birds and mammals endpoints were evaluated for risk in terms of the old parent mixture. Since the ratio of *S* enantiomer is 25% less compared to the new enriched *S* mixture, all effects endpoints for terrestrial mammals and birds would theoretically be lower, thus making RQs lower than those presented in this assessment.

6.2.1 Dietary Concerns to Birds

Agricultural Uses

When indoxacarb is applied to the field at 0.06525 lb a.i./A, with a 3-day application interval and 4 maximum applications per year (

Table 56), there are acute based risk concerns for listed and non-listed species of all avian weight classes, but no subacute or chronic risk concerns. Even after a single application of indoxacarb at this rate acute risk concerns for listed birds remain (**Table 57**).

Following four applications at 0.1125 lb a.i./A with a 3-day application interval, there are both listed and non-listed acute dose based risks, and subacute dietary risk concern for listed birds feeding on short grass (**Table 56**). However, the subacute avian dietary risk LOC for listed species was exceeded at this application rate only for 10 days after the fourth application, suggesting a lower likelihood of an exceedance. The mean Kenaga values, a less conservative estimate, also indicated risk concerns. The lengthening the application interval to 5-days resulted in a similar result. A single application of 0.1125 lbs a.i./ resulted in exceedances of the listed species acute LOC for small and medium sized birds (**Table 57**).

Table 56. Avian RQs using a food item residue approach based on the maximum and mean Kenaga values for indoxacarb for agricultural uses.

	Dose Based RQ LC_{50}=98 mg a.i./kg bw			**Subacute Dietary RQ (LC_{50} = 808 mg/kg-diet)**	**Chronic Dietary RQ (NOAEC= 114 mg/kg-diet)**
	Avian Classes and Body Weights				
	Small 20g	**Mid 100g**	**Large 1000g**		
Foliar Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)					

	Dose Based RQ LC_{50}=98 mg a.i./kg bw Avian Classes and Body Weights			Subacute Dietary RQ (LC_{50} = 808 mg/kg-diet)	Chronic Dietary RQ (NOAEC= 114 mg/kg-diet)
	Small 20g	Mid 100g	Large 1000g		
Food item residue approach					
Short Grass – Max Kenaga (Mean Kenaga)	0.93** (0.33*)	0.41* (0.15*)	0.13* (0.05)	0.07 (0.03)	0.50 (0.18)
Tall Grass– Max Kenaga (Mean Kenaga)	0.42* (0.14*)	0.19* (0.06)	0.06 (0.02)	0.03 (0.01)	0.23 (0.08)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.52** (0.17*)	0.23* (0.08)	0.07 (0.02)	0.04 (0.01)	0.28 (0.09)
Fruits/Pods/Seeds– Max Kenaga (Mean Kenaga)	0.06 (0.03)	0.03 (0.01)	0.01 (0.00)	0.00 (0.00)	0.03 (0.01)
Arthropods– Max Kenaga (Mean Kenaga)	0.36* (0.25*)	0.16* (0.11*)	0.05 (0.04)	0.03 (0.02)	0.20 (0.14)
Granivore– Max Kenaga (Mean Kenaga)	0.01 (0.01)	0.01 (0.00)	0.00 (0.00)	-	-
Foliar Application at 0.1125 lb a.i./acre, 5- day application interval, 4 applications at a maximum application rate of 0.44 lb a.i./acre for cotton and soybeans					
Short Grass– Max Kenaga (Mean Kenaga)	1.51** (0.54**)	0.68** (0.24*)	0.21* (0.08)	0.12* (0.04)	0.82 (0.29)
Tall Grass– Max Kenaga (Mean Kenaga)	0.69** (0.23*)	0.31* (0.10*)	0.10* (0.03)	0.05 (0.02)	0.38 (0.12)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.85** (0.28*)	0.38* (0.13*)	0.12* (0.04)	0.07 (0.02)	0.46 (0.15)
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	0.09 (0.04)	0.04 (0.02)	0.01 (0.01)	0.01 (0.00)	0.05 (0.02)
Arthropods – Max Kenaga (Mean Kenaga)	0.59** (0.41*)	0.27* (0.18*)	0.08 (0.06)	0.05 (0.02)	0.32 (0.22)
Granivore – Max Kenaga (Mean Kenaga)	0.02 (0.01)	0.01 (0.00)	0.00 (0.00)	-	-
Foliar Application at 0.1125 lb a.i./acre, 3- day application interval, 4 applications at a maximum application rate of 0.44 lb a.i./acre for to alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens					
Short Grass– Max Kenaga (Mean Kenaga)	1.60** (0.57**)	0.72** (0.25*)	0.23* (0.08)	0.12* (0.04)	0.87 (0.31)
Tall Grass– Max Kenaga (Mean Kenaga)	0.73** (0.24)	0.33* (0.11)	0.10* (0.03)	0.06 (0.02)	0.40 (0.13)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.90** (0.30)	0.40* (0.13*)	0.13* (0.04)	0.07 (0.02)	0.49 (0.16)
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	0.10* (0.05)	0.04 (0.02)	0.01 (0.01)	0.01 (0.00)	0.05 (0.03)
Arthropods – Max Kenaga (Mean Kenaga)	0.63** (0.43*)	0.28* (0.19*)	0.09 (0.06)	0.05 (0.03)	0.34 (0.24)
Granivore – Max Kenaga (Mean Kenaga)	0.02 (0.01)	0.01 (0.00)	0.00 (0.00)	-	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)

†Exceeds Chronic LOC (≥1.0)

Table 57. Avian RQs using a food item residue approach based on a single application of indoxacarb at the lowest application rate.

	Dose Based RQ LC_{50}=98 mg a.i./kg bw			Subacute Dietary RQ (LC_{50} = 808 mg/kg-diet)	Chronic Dietary RQ (NOAEC= 114 mg/kg-diet)
	Avian Classes and Body Weights				
	Small 20g	Mid 100g	Large 1000g		
Liquid Ground Broadcast and Chemigation Application at 0.06525 lb a.i./acre, 1 application					
Food item residue approach					
Short Grass – Max Kenaga	0.25*	0.11*	0.04	0.02	0.14
Tall Grass– Max Kenaga	0.12*	0.05	0.02	0.01	0.06
Broadleaf plants– Max Kenaga	0.14*	0.06	0.02	0.01	0.08
Fruits/Pods/Seeds– Max Kenaga	0.02	0.01	0.00	0.00	0.01
Arthropods– Max Kenaga	0.10*	0.04	0.01	0.01	0.05
Granivore– Max Kenaga	0.00	0.00	0.00	-	-
Liquid Ground Broadcast and Chemigation Application at 0.1125 lb a.i./acre, 1 application					
Food item residue approach					
Short Grass – Max Kenaga	0.44*	0.20*	0.06	0.03	0.24
Tall Grass– Max Kenaga	0.20*	0.09	0.03	0.02	0.11
Broadleaf plants– Max Kenaga	0.24*	0.11*	0.03	0.02	0.13
Fruits/Pods/Seeds– Max Kenaga	0.03	0.01	0.00	0.00	0.01
Arthropods– Max Kenaga	0.17*	0.08	0.02	0.01	0.09
Granivore– Max Kenaga	0.01	0.00	0.00	-	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
†Exceeds Chronic LOC (≥1.0)

Non-Agricultural Uses

Ground Spray

Acute listed risks were exceeded for small, medium and large birds feeding on short grass, and small and medium sized birds feeding on tall grass, broadleaf plants and arthropods when applied at 0.0375 lbs a.i./A and 12 applications per year (**Table 58**). The only risk scenarios for non-listed species were small birds feeding on short grass and broadleaf plants. For ground spray broadcast at 0.225 lbs a.i./acre findings were similar, with the exception of an additional risk for non-listed medium sized birds feeding on short grass, non-listed small birds feeding on tall grass and non-listed bird feeding on arthropods. Under this scenario, there were now acute listed risks for large birds feeding on arthropods and small birds feeding on fruits/pods and seeds. At the highest application rate considerably more acute risks were triggered for non-listed species including all sized birds feeding on short grass, broadleaf plants, and arthropods. Non-listed risks were triggered for small and medium birds feeding on fruits/pods and seeds and listed large birds feeding on fruits/pods and seeds. For granivores, the only risk pictures were for listed small and medium birds. Overall, there were no chronic risks to birds except at the highest non-agricultural application rate.

Table 58. Avian RQs based on the maximum and mean Kenaga values for Indoxacarb for non-agriculture uses.

	Dose Based RQ **LC_{50}=98 mg a.i./kg bw**			**Subacute Dietary RQ** **(LC_{50} = 808 mg/kg-diet)**	**Chronic Dietary RQ** **(NOAEC= 114 mg/kg-diet)**
	Avian Classes and Body Weights				
	Small **20g**	**Mid** **100g**	**Large** **1000g**		
Foliar Application at 0.0375 lb a.i./acre, 7-day application interval and 12 applications per year at a maximum annual rate of 0.45 lbs a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf					
Short Grass – Max Kenaga (Mean Kenaga)	0.91** (0.32*)	0.41* (0.14*)	0.13* (0.05)	0.07 (0.02)	0.49 (0.18)
Tall Grass– Max Kenaga (Mean Kenaga)	0.42* (0.14)	0.19* (0.06)	0.06 (0.02)	0.03 (0.01)	0.23 (0.07)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.51** (0.17)	0.23* (0.08)	0.07 (0.02)	0.04 (0.01)	0.28 (0.09)
Fruits/Pods/Seeds– Max Kenaga (Mean Kenaga)	0.06 (0.03)	0.03 (0.01)	0.01 (0.00)	0.00 (0.00)	0.03 (0.01)
Arthropods– Max Kenaga (Mean Kenaga)	0.36* (0.25*)	0.16* (0.11*)	0.05 (0.03)	0.03 (0.02)	0.19 (0.13)
Granivore– Max Kenaga (Mean Kenaga)	0.01 (0.01)	0.01 (0.00)	0.00 (0.00)	-	-
Foliar Application 0.225 lb a.i./acre, 7-day application interval and 2 maximum applications per year at a maximum annual rate of 0.45 lb a.i./acre for ornamental lawns and turf.					
Short Grass– Max Kenaga (Mean Kenaga)	1.63** (0.58**)	0.73** (0.26)	0.23* (0.08)	0.23 (0.04)	0.89 (0.31)
Tall Grass– Max Kenaga (Mean Kenaga)	0.75** (0.24*)	0.33* (0.11*)	0.11* (0.03)	0.06 (0.02)	0.41 (0.13)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.92** (0.31*)	0.41* (0.14*)	0.13* (0.04)	0.07 (0.02)	0.50 (0.17)
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	0.10* (0.05)	0.05 (0.02)	0.01 (0.01)	0.01 (0.00)	0.06 (0.03)
Arthropods – Max Kenaga (Mean Kenaga)	0.64** (0.44*)	0.29* (0.20*)	0.09 (0.06)	0.05 (0.03)	0.35 (0.24)
Granivore – Max Kenaga (Mean Kenaga)	0.02 (0.01)	0.01 (0.00)	0.00 (0.00)	-	-
Ground spray broadcast at 1.437 lb a.i./acre, 7-day application interval and 12 maximum applications for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites					
Short Grass– Max Kenaga (Mean Kenaga)	34.83** (12.34**)	15.60** (5.53)	4.95** (1.75**)	2.67† (0.95)	18.94† (6.71†)
Tall Grass– Max Kenaga (Mean Kenaga)	15.97** (5.23**)	7.15** (2.34)	2.27** (0.74**)	1.22† (0.40)	8.68† (2.84)
Broadleaf plants– Max Kenaga (Mean Kenaga)	19.59** (6.53**)	8.78** (2.93)	2.78** (0.93**)	1.50† (0.50)	10.66† (3.55†)

	Dose Based RQ LC$_{50}$=98 mg a.i./kg bw			Subacute Dietary RQ (LC$_{50}$ = 808 mg/kg-diet)	Chronic Dietary RQ (NOAEC= 114 mg/kg-diet)
	Avian Classes and Body Weights				
	Small 20g	Mid 100g	Large 1000g		
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	2.18** (1.02**)	0.98** (0.46)	0.31* (0.14*)	0.17 (0.08)	1.18† (0.55)
Arthropods – Max Kenaga (Mean Kenaga)	13.64** (9.43**)	6.11** (4.23**)	1.94** (1.34**)	1.05† (0.72)	7.42† (5.13†)
Granivore – Max Kenaga (Mean Kenaga)	0.48* (0.23)	0.22* (0.10)	0.07 (0.03)	-	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
†Exceeds Chronic LOC (≥1.0)

6.2.2 Dietary Concerns to Mammals

Agricultural Uses

Overall, there were minimal acute risks to mammals for agricultural uses. When indoxacarb is applied to the field at 0.06525 lb a.i./acre, with a 3-day application interval and 4 maximum applications per year (Table 59**Table 60**), there is only an acute concern for small listed mammals feeding on short grass. On a chronic basis, there were dose based risk concerns for mammals of all size classes feeding on short grass, tall grass, broadleaf plants and arthropods, but no chronic concerns for mammals feeding on fruits/pods and seeds and granivores. The only chronic dietary risk of concern was mammals feeding on short grass.

Four applications at 0.1125 lb a.i./acre, with a 5-day application interval, result in acute risks to listed mammals for a few cases (**Table 59**). There are acute concerns for small, medium and large mammals feeding on short grass, small mammals feeding on tall grass, and small and medium mammals feeding on broadleaf plants. There are chronic risk concerns for almost all size classes and feeding guilds in this application scenario except for granivores and large mammals feeding on fruits/pods and seeds.

At the application scenario using the maximum labeled rate for agricultural uses, there were still minimal acute risks and again, only to listed mammals. There were acute risk concerns for small medium and large mammals feeding on short grass and small mammals feeding on tall grass and broadleaf plants.

A few additional modeling considerations were taken to address the certainty in the chronic risk concern. First, even with a single application of indoxacarb to agricultural crops at 0.0625 lb a.i./acre, there were chronic dose based risk concerns for several size classes and feeding guilds of mammals (**Table 60**). Second, looking at less conservative mean Kenaga values in the T-REX output also support a consistent pattern of chronic risk exceedances at all application rates (Table 59). Third, after the first application at 0.1125 lb a.i./acre, the LOCs for all listed species (15g, 35g, and 100g) is exceeded for all feeding groups and guilds and remains exceeded until approximately 78 days post all 4 applications. Even LOCs for non-listed species remain exceeded after the fourth application for all feeding groups except for arthropods and fruits/pods and seeds and remains exceeded until approximately 70 days post application.

Table 59. Mammalian RQs for Indoxacarb applied to cotton and soybeans

	Acute Dose-based RQ (Adjusted LD_{50}) LD_{50}=179 mg/kg-bw			Chronic Dose Based RQ (Adjusted NOAEL)			Chronic Dietary RQ NOAEC = 40 (ppm)
	Mammal Size Classes and Body Weights			Mammal Size Classes and Body Weights			
	Small 15 g	Mid 35g	Large 1000g	Small 15 g	Mid 35 g	Large 1000g	
Foliar Application at 0.06525 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.261 lb a.i./acre for sweet corn, okra, leafy vegetables, mint/peppermint/spearmint, and brassica (head and stem vegetables)							
Short Grass-Max Kenaga (Mean Kenaga)	0.13* (0.05)	0.11 (0.04)	0.06 (0.02)	11.93† (4.23†)	10.19† (3.61)	5.46† (1.93†)	1.38† (0.49)
Tall Grass Max Kenaga (Mean Kenaga)	0.06 (0.02)	0.05 (0.02)	0.03 (0.01)	5.47† (1.79†)	4.67† (1.53†)	2.50† (0.82)	0.63 (0.21)
Broadleaf plants Max Kenaga (Mean Kenaga)	0.07 (0.02)	0.06 (0.02)	0.03 (0.01)	6.71† (2.24†)	5.73† (1.91†)	3.07† (1.02†)	0.77 (0.26)
Fruits/pods/Seeds Max Kenaga (Mean Kenaga)	0.01 (0.00)	0.01 (0.00)	0.00 (0.00)	0.75 (0.35)	0.64 (0.30)	0.34 (0.16)	0.09 (0.04)
Arthropods Max Kenaga (Mean Kenaga)	0.05 (0.04)	0.04 (0.03)	0.02 (0.02)	4.67† (3.23)	3.99† (2.76†)	2.14† (1.48†)	0.54 (0.37)
Granivores Max Kenaga (Mean Kenaga)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.17 (0.08)	0.14 (0.07)	0.08 (0.04)	-
Foliar Application at 0.1125 lb a.i./acre, 5- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for cotton and soybeans							
Short Grass-Max Kenaga (Mean Kenaga)	0.23* (0.08)	0.19* (0.07)	0.10* (0.04)	20.32† (7.20†)	17.35† (6.15†)	9.30† (3.29†)	2.34† (0.83)
Tall Grass Max Kenaga (Mean Kenaga)	0.10* (0.03)	0.09 (0.03)	0.05 (0.02)	9.31† (3.05†)	7.95† (2.60†)	4.26† (1.40†)	1.07† (0.35)
Broadleaf plants Max Kenaga (Mean Kenaga)	0.13* (0.04)	0.11* (0.04)	0.06 (0.02)	11.43† (3.81†)	9.76† (3.25†)	5.23† (1.74†)	1.32† (0.44)
Fruits/pods/Seeds Max Kenaga (Mean Kenaga)	0.01 (0.01)	0.01 (0.01)	0.01 (0.00)	1.27† (0.59)	1.08† (0.51)	0.58 (0.27)	0.15 (0.07)
Arthropods Max Kenaga (Mean Kenaga)	0.09 (0.06)	0.08 (0.05)	0.04 (0.03)	7.96† (5.50†)	6.80† (4.70†)	3.64† (2.52†)	0.92 (0.63)
Granivores Max Kenaga (Mean Kenaga)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.28 (0.13)	0.24 (0.11)	0.13 (0.06)	-
Foliar Application at 0.1125 lb a.i./acre, 3- day application interval, 4 applications at a maximum seasonal application rate of 0.44 lb a.i./acre for to alfalfa, beans (dried type, succulent, except soybean), beets, cucurbit vegetables, grapes, cranberries, low growing berries, bushberries, small fruit vine climbing							

subgroup (except fuzzy kiwi fruit), peanuts, pome fruit, root and tuber vegetables (potato), stone fruits and leafy greens							
Short Grass-Max Kenaga (Mean Kenaga)	0.24* (0.08)	0.20* (0.07)	0.11* (0.04)	21.48† (7.61†)	18.34† (6.50†)	9.83† (3.48†)	2.48† (0.88)
Tall Grass Max Kenaga (Mean Kenaga)	0.11* (0.04)	0.09 (0.03)	0.05 (0.02)	9.84† (3.22†)	8.41† (2.75)	4.51† (1.47†)	1.13† (0.37)
Broadleaf plants Max Kenaga (Mean Kenaga)	0.13* (0.04)	0.12 (0.04)	0.06 (0.02)	12.08† (4.03†)	10.32† (3.44†)	5.53† (1.84†)	1.39† (0.46)
Fruits/pods/Seeds Max Kenaga (Mean Kenaga)	0.01 (0.01)	0.01 (0.01)	0.01 (0.00)	1.34† (0.63)	1.15† (0.54)	0.61† (0.29)	0.15 (0.07)
Arthropods Max Kenaga (Mean Kenaga)	0.09 (0.06)	0.08 (0.06)	0.04 (0.03)	8.41† (5.82†)	7.18† (4.97†)	3.85† (2.66†)	0.97 (0.67)
Granivores Max Kenaga (Mean Kenaga)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.30 (0.14)	0.25 (0.12)	0.14 (0.06)	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
[+]Exceeds Chronic LOC (≥1.0)

Table 60. Mammalian RQs based on a single application of indoxacarb at the lowest application rate for agricultural uses.

	Acute Dose-based RQ (Adjusted LD_{50}) LD_{50}=179 mg/kg-bw			Chronic Dose Based RQ (Adjusted NOAEL)			Chronic Dietary RQ
	Mammal Size Classes and Body Weights			Mammal Size Classes and Body Weights			NOAEC = 40 (ppm)
	Small 15 g	Mid 35g	Large 1000g	Small 15 g	Mid 35 g	Large 1000g	
Foliar Application at 0.06525 lb a.i./acre, 1 application							
Food item residue approach							
Short Grass– Max Kenaga	0.04	0.03	0.02	3.40†	2.90†	1.56†	0.39
Tall Grass – Max Kenaga	0.02	0.01	0.01	1.56†	1.33†	0.71	0.18
Broadleaf plants– Max Kenaga	0.02	0.02	0.01	1.91†	1.63†	0.87	0.22
Fruits/pods/Seeds– Max Kenaga	0.00	0.00	0.00	0.21	0.18	0.10	0.02
Arthropods– Max Kenaga	0.01	0.01	0.01	1.33†	1.14†	0.61	0.15
Granivores– Max Kenaga	0	0	0	0.05	0.04	0.02	-
Foliar Application at 0.1125 lb a.i./acre, 1 application							
Food item residue approach							
Short Grass– Max Kenaga	0.07	0.06	0.03	5.86†	5.00†	2.68†	0.68
Tall Grass – Max Kenaga	0.03	0.03	0.01	2.68†	2.29†	1.23†	0.31
Broadleaf plants– Max Kenaga	0.04	0.03	0.02	3.29†	2.81†	1.51†	0.38
Fruits/pods/Seeds– Max Kenaga	0.00	0.00	0.00	0.37	0.31	0.17	0.04
Arthropods– Max Kenaga	0.03	0.02	0.01	2.29†	1.96†	1.05†	0.26
Granivores– Max Kenaga	0.00	0.00	0.00	0.08	0.07	0.04	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
[+]Exceeds Chronic LOC (≥1.0)

Non-Agricultural Uses

On a chronic basis, mammalian LOCs were exceeded for almost all size classes on both a chronic dose base and dietary basis. For the lowest application rate (0.0375 lb a.i./acre), there were minimal risks on an acute basis. The only acute risk was for listed small and medium listed mammals feeding on short grass. However, chronic risk LOCs were exceeded for all size classes and feeding guilds except for mammals feeding on fruits/pods and seeds and granivores. Chronic dietary risk was only exceeded for mammals feeding on short grass.

At the next highest non-agricultural application rate (0.225 lb a.i./acre), the LOC was only exceeded on an acute basis for listed small, medium and large mammals feeding on short grass, and small and medium mammals feeding on tall grass and broadleaf plants. Again chronic risks were exceeded for all sizes and feeding groups except granivores.

At the highest non-agricultural application rate (1.437 lb a.i./acre), there were acute risks to both listed and non-listed mammals. Acute non-listed small medium and large mammals triggered risk concerns from short grass, tall grass, and arthropod feeding guilds, but only listed concerns for mammals from broadleaf plants and fruit/pods/seeds feeding guilds.

Again, for non-agricultural scenarios, several lines of evidence support chronic risk exceedances. First, the mean Kenaga values are also exceeded for many chronic risk scenarios. Second, RQs associated with residues on mammalian dietary items don't drop below the LOC until approximately 120 days post application for fruits/pods/seeds, and 320 days for short grass and other plants. Thus there is a potential for chronic exposure that could elicit effects for a period of months after application, which may coincide with the reproductive period of the bird.

Overall, for mammals, chronic dose based RQs were calculated based on a 15-day developmental dietary toxicity test in which the NOAEC was 40 mg a.i./kg based on reduced fetal weight. Due to the lack of a true 2-generation reproductive study in mammals, we may be underestimating chronic risk. Hemolytic effects in rats were also seen in several studies at lower doses (8 - 10 mg/kg-bw); however, it is unclear how these effects translate into risk concerns for survival and reproduction for wild mammals.

Table 61 . Mammalian RQs based on the maximum and mean Kenaga values for Indoxacarb for non-agriculture uses.

	Dose Based RQ LD_{50}=179 mg/kg-bw			**Chronic Dose Based (RQ) (Adjusted NOAEL)**			**Chronic Dietary RQ (NOAEC= 40 (ppm)**
	Mammal Size Classes and Body Weights			**Mammal Size Classes and Body Weights**			
	Small 15g	**Mid 35g**	**Large 1000g**	**Small 15g**	**Mid 35g**	**Large 1000g**	
Foliar Application 0.0375 lb a.i./acre, 7-day application interval and 12 applications per year at a maximum seasonal rate of 0.45 lbs a.i./acre for commercial/institutional/industrial premises/equipment, recreational areas, households domestic dwellings, non-agricultural uncultivated areas/soils, and golf course turf							

	Dose Based RQ LD50=179 mg/kg-bw			Chronic Dose Based (RQ) (Adjusted NOAEL)			Chronic Dietary RQ (NOAEC= 40 (ppm)
	Mammal Size Classes and Body Weights			Mammal Size Classes and Body Weights			
	Small 15g	Mid 35g	Large 1000g	Small 15g	Mid 35g	Large 1000g	
Short Grass – Max Kenaga (Mean Kenaga)	0.14* (0.05)	0.12* (0.04)	0.06 (0.02)	12.22† (4.33)	10.44† (3.70)	5.60† (1.98)	1.41† (0.50)
Tall Grass– Max Kenaga (Mean Kenaga)	0.06 (0.02)	0.05 (0.02)	0.03 (0.01)	5.60† (1.83)	4.79† (1.57)	2.57† (0.84)	0.65 (0.21)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.08 (0.03)	0.07 (0.02)	0.04 (0.01)	6.88† (2.29)	5.87† (1.96)	3.15† (1.05)	0.79 (0.26)
Fruits/Pods/Seeds– Max Kenaga (Mean Kenaga)	0.01 (0.00)	0.01 (0.00)	0.00 (0.00)	0.76 (0.36)	0.65 (0.30)	0.35 (0.16)	0.09 (0.04)
Arthropods– Max Kenaga (Mean Kenaga)	0.05 (0.04)	0.05 (0.03)	0.02 (0.02)	4.79† (3.31)	4.09† (2.83)	2.19† (1.52)	0.55 (0.38)
Granivore– Max Kenaga (Mean Kenaga)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.17 (0.08)	0.15 (0.07)	0.08 (0.04)	-
Foliar Application 0.225 lb a.i./acre, 7-day application interval and 2 maximum applications per year at a maximum seasonal rate of 0.45 lb a.i./acre for ornamental lawns and turf							
Short Grass– Max Kenaga (Mean Kenaga)	0.24* (0.09)	0.21* (0.07)	0.11* (0.04)	21.91† (7.76)	18.71† (6.63)	10.03† (3.55)	2.53† (0.89)
Tall Grass– Max Kenaga (Mean Kenaga)	0.11* (0.04)	0.10* (0.03)	0.05 (0.02)	10.04† (3.29)	8.58† (2.81)	4.60† (1.50)	1.16† (0.38)
Broadleaf plants– Max Kenaga (Mean Kenaga)	0.14* (0.05)	0.12* (0.04)	0.06 (0.02)	12.32† (4.11)	10.53† (3.51)	5.64† (1.88)	1.42† (0.47)
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	0.02 (0.01)	0.01 (0.01)	0.01 (0.00)	1.37† (0.64)	1.17† (0.55)	0.63† (0.29)	0.16 (0.07)
Arthropods – Max Kenaga (Mean Kenaga)	0.10 (0.07)	0.08 (0.06)	0.04 (0.03)	8.58 (5.93)	7.33† (5.07)	3.93† (2.72)	0.99 (0.68)
Granivore – Max Kenaga (Mean Kenaga)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.30* (0.14*)	0.26 (0.12)	0.14 (0.07)	-
Foliar Application at 1.437 lb a.i./acre, 7-day application interval and 12 maximum applications for commercial/institutional/industrial premises/equipment, household domestic dwellings and refuse and solid waste sites							
Short Grass– Max Kenaga (Mean Kenaga)	5.23** (1.85**)	4.47** (1.58**)	2.40** (0.85**)	468.38† (165.9†)	400.09† (141.7†)	214.46† (75.96†)	53.99† (19.12†)
Tall Grass– Max Kenaga (Mean Kenaga)	2.40** (0.79**)	2.05** (0.67**)	1.10** (0.36*)	214.68† (70.26†)	183.37† (60.01†)	98.30† (32.17)	24.74† (8.10†)
Broadleaf plants– Max Kenaga (Mean Kenaga)	2.94** (0.98**)	2.51** (0.84**)	1.35** (0.45*)	263.47† (87.8†)	225.05† (75.0†)	120.64† (40.2†)	30.37† (10.12†)
Fruits/Pods/Seeds – Max Kenaga (Mean Kenaga)	0.33* (0.15*)	0.28* (0.17*)	0.15* (0.07)	29.27† (13.7†)	25.01† (11.67†)	13.40† (6.26)	83.37† (1.57†)
Arthropods – Max Kenaga (Mean Kenaga)	2.05** (1.42**)	1.75** (1.21**)	0.94** (0.65**)	183.45† (126.8†)	156.70† (108.4†)	84.00† (58.1†)	21.14† (14.62†)
Granivore – Max Kenaga (Mean Kenaga)	0.07 (0.03)	0.06 (0.03)	0.03 (0.02)	6.51† (3.04†)	5.56† (2.59†)	2.98† (1.39†)	-

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
[+]Exceeds Chronic LOC (≥1.0)

6.2.3 Spray Drift Analysis for Chronic Risk to Mammals

The footprint of off-field spray drift from the agricultural field was investigated for both birds and mammals following the Environmental Fate and Effects Division Offsite Transport Guidance (USEPA, 2013b). The fraction of applied for terrestrial animals was calculated using risk quotients from T-REX that reflect the maximum application rate and maximum number of agricultural applications, and compared to the LOC. Drift resulting from multiple applications may increase the probability of offsite dietary exposure to wildlife. AgDRIFT version 2.1.1 was used to model the drift distance (*i.e.,* the distance extending from the edge of the field out to where the mammalian chronic RQ exceeds the LOC) following a single application at 0.0625 or 0.1125 lbs a.i./A. The distances provided in **Table 62** are based on the maximum chronic non-listed risk quotient (3.4 and 5.86 for the two rates respectively). The analysis suggests that the mammalian chronic LOC may be exceeded between 16 and 348 ft from the edge of the treated field for aerial applications, and less than 95 feet for modeled ground applications. When modeling multiple spray drift events the assumptions include the wind is blowing at the same speed in the same direction.

Due to low acute RQs for birds, the spray drift analysis indicated a drift distance of 0 ft for acute risks. Since there are no chronic agricultural risk concerns on-field, chronic risks associated with spray drift were not assessed.

Table 62. Spray drift distances to the non-listed mammalian chronic LOC for agricultural uses.

	Aerial Spray Drift Distance to Exceed non-listed chronic LOCs (ft)	***Ground Application Drift Distance Exceed non-listed chronic LOCs (ft)***			
Application Rate		***Low Boom Very fine to Fine***	***Low Boom Fine to Medium***	***High Boom Very Fine to Fine***	***High Boom Fine to Medium***
0.06525 lb a.i./acre	16	3	10	3	3
0.06525 lb a.i./acre x 4 applications	115	13	3	33	7
0.06525 lb a.i./acre x 4 applications x 4 seasons	203	20	7	56	13
0.1125 lb a.i./acre	52	7	10	3	3
0.1125 lb a.i./acre x 4 applications	197	20	7	56	10
0.1125 lb a.i./acre x 4 applications x 4 seasons	348	36	13	95	20

6.2.4 Granular Uses for Birds and Mammals

The application of Adivon Insect Granule, is representative of the granular forms of indoxacarb used to control fire ants and other pests including mole crickets. The granule can be applied at 2 application rates (0.11 lbs a.i./acre and 0.44 lbs a.i./acre). This assessment assumed a single granular assessment, although the label did not have a specific application interval, it says to apply as needed. The label specified soil incorporation will decrease the efficacy of the granule; this assessment did not look at effects of incorporation to various depths. The LD_{50}/ft^2 approach indicates risks of concern for the two granular application rates for non-listed small avian and mammalian size classes. Application rates are based on the average weight of an indoxacarb Adivon insect granule (EPA Reg.# 100-1483, 69.4 ± 13.1 mg), at 0.22% active ingredient in the product (e-mail from Monty Dixon of Syngenta to Jill Bloom PRD, on March 16, 2017). One 20g bird, consuming <1 granule would exceed the listed avian LOC (0.1) assuming a 10% foraging efficiency (**Table 63-64)**. The attractiveness of the granules to mammals and birds may be dependent on the color or size of the granule which may become confused as an insect or grit, but this analysis indicates that even the accidental consumption of less than one granule will reach the LOC. However, for smaller passerine species, consuming an entire Adivon fire ant granule is unlikely due to the granule size relative to the bird size (Benkman and Pulliam, 1988). Adivon insect granules have a variety of application uses and locations that may either leave a small or large footprint. Specifically, there are no effects studies with the Adivon fire ant granule for birds or mammals. However, based on extrapoliations from other effects studies, the risk to birds and mammals is likely but dependent on the availability of the granule, and the number and density of treated areas across the landscape. The likelihood of this occurring will depend on the granule size relative to size and foraging patterns of birds and mammals.

Table 63. Avian RQs for the granular formulation of indoxacarb

	Dose Based RQ		
	Avian Classes and Body Weights		
	Small 20g	Mid 100g	Large 1000g
Granular application rate of 0.1101 lb a.i./acre for commercial/institutional/industrial premises and equipment, LD_{50}/sq ft approach			
	0.81**	0.13*	0.01
Granular and perimeter granule application rate of 0.44 lb a.i./acre for golf course turf, and household domestic dwellings, LD_{50}/sq ft approach			
	3.24**	0.51*	0.04

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)

Table 64. Mammalian RQs for the granular formulation of indoxacarb applied to golf course turf, ornamental laws and turf, and household and domestic dwellings.

	Dose Based RQ		
	Avian Classes and Body Weights		
	Small 15g	**Mid 35g**	**Large 1000g**
Granular application rate of 0.1101 lb a.i./acre for commercial/institutional/industrial premises and equipment, LD_{50}/sq ft approach			
	0.89**	0.47*	0.04
Granular and perimeter granule application rate of 0.44 lb a.i./acre for golf course turf, and household domestic dwellings, LD_{50}/sq ft approach			
	0.78**	0.41*	0.03

[1]The below notation will be used to denote values that exceed the Levels of Concern (LOC)
*Exceeds Acute Listed LOC (≥ 0.1)
**Exceeds Acute Non-Listed LOC (≥0.5)
†Exceeds Chronic LOC (≥1.0)

Table 65. Estimation of granules and foraging area required to exceed avian and mammalian LOCs.

	Birds (20g)	**Mammals (15g)**
No. of granules needed to achieve LD50	9.25 granules	38.65 granules
No. of granules needed to achieve the LOC of 0.5 (1/2 LD50)	4.62 granules	19.33 granules
No. of granules needed to achieve the LOC of 0.1 (1/10 LD50)	0.92 granules	3.87 granules
Foraging area needed to achieve ingestion of sufficient mass to exceed listed species LOC assuming 10% foraging efficiency	0.31 ft^2	1.29 ft^2

6.2.4 Bioaccumulation in Birds and Mammals

The consumption of aquatic organisms that have accumulated indoxacarb may serve as an additional exposure route for higher trophic level organisms. Potential risks to birds and mammals that consume aquatic organisms were evaluated using KABAM (v 1.0). A suite of scenarios was run using the 14-day pore and water column EECs (steady state) for both indoxacarb parent and the total toxic residues (TTR). Bioaccumulation is a pathway of concern because of indoxacarb's high bioconcentration factor of up to 1315X in whole bluegill sunfish (MRID 44477319, 45805301) and octanol-water partition coefficient (Log K_{ow} = 4.65). A bioconcentration and metabolism study in fish exposed to water treated with DPX-JW062 (MRID 44477319), noted the preferential accumulation of the IN-JT333 enantiomer in fish fillet, viscera, and whole fish tissues (via metabolism of the parent indoxacarb in fish).

First, the parent EECs were evaluated for bioaccumulation potential using KABAM. The concentrations for parent in both the water column and pore water were modeled for both single and multiple seasons at each application interval. For agricultural uses, one use pattern (application to leafy vegetables: 0.11 lbs a.i./A x 4 apps aerially applied for 4 seasons with a 3-day application interval) resulted in acute risks to species that consume benthic invertebrates, filter feeders and small fish (e.g., sandpipers). Chronic exposure risks were identified for mammals consuming fish (i.e., river otters) for cotton, soybean and leafy vegetables. Chronic risks were also identified for other mammals (shrews, rice rat, star-nosed mole, mink) that consume benthic invertebrates, filter feeders and fish from the highest use scenario (application to leafy vegetables: 0.11 lbs a.i./A x 4 apps aerially applied for 4 seasons with a 3-day application interval). For the non-agricultural turf use, there were no risk concerns, for wildlife consuming contaminated prey.

To account for the degradation of indoxacarb into the highly bioaccumulative degradate IN-JT333 (log k_{ow}=5.0, estimate from Episuite), a TTR approach was taken using the most conservative chemical fate properties for indoxacarb and its degradates and the most sensitive effects data. TTR EECs were calculated for the minimum and maximum parent exposure scenarios (**Table 67**) and modeled in KABAM (i.e., CA lettuce and CA Cotton). For the two agricultural use scenarios modeled, both use patterns resulted in acute risk for mammals consuming fish and invertebrates (e.g., river otters, shrews) for cotton and lettuce. For mammals, chronic dose based risk exposures were identified for mink, otters, shrews, and moles for both cotton and lettuce (0.11 lbs a.i./A x 4 aerial applications with a 3 and 5-day application interval respectively).

Overall, pore water and water column EECs are similar for the indoxacarb parent and the TTR. However, when modeling the TTR in KABAM using the most conservative approach, endpoints were converted to “indoxacarb units”. There is a large variation of differential toxicity between indoxacarb parent and its degradates. The degradate, IN- JT333 is much more highly toxic in mammals compared to birds and the indoxacarb parent on an acute basis. Thus, the exposure of mammals to IN-JT333 has much greater risk concern on an acute basis compared to the parent. Because of the multiple applications aquatic wildlife exposure to indoxacarb will persist throughtout the season of application; therefore, despite the rapid depuration concentrations of indoxacarb in fish are likely to remain constant.

Table 66. KABAM Modeling Results for Indoxacarb Parent

Crop	Application Rate, Method, and Interval	PWC Scenario	14-day Pore Water Concentration (µg/L)	14-day Water Column Concentration (µg/L)	Risk Concern[1]	
					Acute	Chronic
Indoxacarb						
Cotton	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0004	1.17	Acute RQs < 0.1	Chronic RQs < 1.0
		MS Cotton	0.001	2.25	Acute RQs < 0.1	Chronic Dose Based Risk for small and large river otters (RQs: 1.0-1.3)
		NC Cotton	0.0012	2.09	Acute RQs <0.1	Chronic Dose Based Risk for large river otters (RQ: 1.220)
	0.11 lbs a.i./A x 4 Ground 5-day interval	CA Cotton	0.0004	0.65	Acute RQs < 0.1	Chronic RQs < 1.0
		MS Cotton	0.0009	2.19	Acute RQs < 0.1	Chronic dose based Risk for large river otter (RQ: 1.28)
		NC Cotton	0.0011	1.86	Acute RQs < 0.1	Chronic dose based Risk for large river otter (RQ: 1.09)
Soybean	0.11 lbs a.i./A x 4 Aerial 5-day interval	MS Soybean	0.0008	1.77	Acute RQs < 0.1	Chronic dose based Risk for large river otter (RQ: 1.03)
	0.11 lbs a.i./A x 4 Ground 5-day interval	MS Soybean	0.0006	1.35	Acute RQs < 0.1	Chronic RQs < 1.0
Leafy Vegetables	0.11 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0023	4.36	Acute Risk for sandpipers (RQ: 0.106)	Chronic dose based risk for rice rate/star-nosed mole, small mink, large mink, small and large river

Crop	Application Rate, Method, and Interval	PWC Scenario	14-day Pore Water Concentration (µg/L)	14-day Water Column Concentration (µg/L)	Risk Concern[1]	
					Acute	Chronic
						otter (RQ: 1.22-2.54)
	0.065 lbs a.i./A x 4 Aerial 3-day interval 4 seasons	CA Lettuce	0.0014	2.56	Acute RQs < 0.10	Chronic Dose based risk for large mink and small and large river otters (RQ: 1.07-1.50)
	0.11 lbs a.i./A x 4 Aerial 3-day interval 1 season	CA Lettuce	0.0007	1.65	Acute RQs < 0.1	Chronic RQs < 1.0
Non-Agricultural Turf						
Turf	0.44 lbs a.i./A x 1 Ground	PA Turf	0.0003	0.81	Acute RQs < 0.1	Chronic RQs < 1.0
		FL Turf	0.0002	0.75	Acute RQs < 0.1	Chronic RQs < 1.0

[1]Acute LOC for birds and mammals=0.1; Chronic LOC for birds and mammals=1.0

Table 67. KABAM Modeling Results for Indoxacarb TTR

Crop	Application Rate, Method, and Interval	PWC Scenario	14-day Pore Water Concentration (µg/L)	14-day Water Column Concentration (µg/L)	Risk Concern[1]	
					Acute	Chronic
Estimated TTR[2]						
Leafy Vegetables	0.11 lbs a.i./A x 4 Aerial 5-day interval	CA Cotton	0.0005	1.25	Acute Dose Based Risk for Large River Otter (RQ: 0.118)	Chronic Dose Based Risk for small mink, large mink, small river otter, large river otter (RQ: 1.14-2.05)
	0.11 lbs a.i./A x 4 Aerial	CA Lettuce	0.0024	4.41	**Acute Dose Based Risk for fog/water shrew, rice rat/star-**	**Chronic dose based Risk for fog/water shrew, rice rat/star-**

	3-day interval 4 seasons				**nosed mole, small mink, large mink, small river otter, large river otter (RQ: 0.119-0.417)** **Acute Dose Based risk for sandpipers and rails (RQ:0.227-0.124)**	**nosed mole, small mink, large mink, small river otter, large river otter (RQ: 2.06-7.24)**

[1]Acute LOC for birds and mammals=0.1; Chronic LOC for birds and mammals=1.0
[2]The estimated TTR is a summation of the individual PWC concentration time series (not adjusted for toxicity ratios) as modeled for the TEQ process, followed by the 1 in 10-year estimation.

6.2.5 Drinking Water and Inhalation Risk

STIR can be used to provide an upper bound estimate of exposure of birds and mammals to indoxacarb through inhalation of spray drift or vapor. This screen indicates that spray droplet exposure from indoxacarb is not likely significant for birds or mammals. The model estimates avian-inhalation toxicity values, when not directly available, from mammalian data by applying an adjustment factor representing the difference in lung tissue thickness and surface area between birds and mammals to the relationship between mammalian-oral, mammalian-inhalation, and avian-oral toxicity values to account for differences in avian and mammalian inhalation toxicity. This model was run in the Problem Formulation (USEPA 2013a) and the weight-of evidence suggested low risk to birds and mammals from vapor phase inhlation based on the available data and taking into consideration that the screen assumes 100% air saturation.

SIP was used to determine an upper bound estimate of bird and mammal exposure to indoxacarb in drinking water (based on a indoxacarb concentration in water assumed to be at solubility limit in water 0.8 mg/L at 25ºC).   The screening suggests that there are no chronic or acute risk concerns for both birds and mammals. This screening is qualitative, is based on drinking water exposure alone, and is based on several conservative assumptions which add considerable uncertainty to this risk conclusion. This model was run in the Problem Formulation (USEPA 2013a). which suggested that drinking water alone is not a potential concern for birds or mammals.

6.3 Risk Concerns to Honeybees

The risk estimation process involves a quantitative Tier I assessment of the potential for risk to individual bees. This exposure potential is a function of the application method, timing, location (*e.g.*, indoor vs. outdoor), the attractiveness of the crop to bees, agronomic practices (*e.g.*, timing of harvest), and the availability of alternative forage sources. For informing the potential for exposure of bees to indoxacarb on the treated site, information on the attractiveness of crops was considered based on USDA[10] compilations (**Table 26**).

Tier I RQs Agricultural and Non-Agricultural Uses-Oral Exposure

For oral (dietary) exposure, the Tier I assessment initially considers just the caste of bees with the greatest oral exposure (foraging adults). If risks are identified, then other factors are considered for refining the default Tier I risk estimates. These factors include other castes of bees and available information on residues in pollen and nectar which are deemed applicable to the crops of interest. Oral exposure through the consumption of indoxacarb-contaminated pollen is considered for on-field and off-field scenarios resulting from foliar applications. For soil applications, where no spray drift is expected, oral exposure is assessed for the on-field scenario only.

For foliar applications, the Bee-REX model uses a standard dose of 32 µg a.i./bee per 1 lbs. a.i./A for adults and 13.6 µg a.i./bee for larvae that are based off of consumption rates for these life stages. This dose is multiplied by the application rate to yield an oral dose, one each for adults and larvae. For indoxacarb, this dose is compared against the most sensitive acute oral LD50 value of 0.068 ug a.i./bee for adult acute exposure. No data were provided for adult chronic exposure. For larvae, the available acute oral toxicity study resulted in an LD50 of 18.1 ug a.i./bee and a chronic NOAEL of 0.0168 ug a.i./bee.

For the non-agricultural soil applications, the oral exposure estimate for adults and larvae are determined using Briggs model estimates (based off application rate, the log KOW, and organic carbon partition coefficient KOC of indoxacarb) multiplied by the consumption rates of 0.292 g/day for adults and 0.124 g/day for larvae. The exposure estimates are compared against the same endpoints as described above.

Table 68 summarizes the acute and chronic RQs resulting from foliar and soil applications of indoxacarb. For foliar applications, the acute and chronic RQs for adult bees exceed the LOC of 0.4 and 1.0 respectively for all use patterns (RQs range from 10.28 to 91.04). The acute and chronic RQs are also above the LOC for all use patterns with the exception of the acute RQ for larval exposure when indoxacarb is applied at an application rate of 0.06525 lbs a.i./acre. For soil applications, the only exceedances were acute adult and chronic larvae LOCs at the highest non-agricultural application rate of 1.437 lbs a.i./acre which represents perimter sprays at Commercial/institutional/ industrial premises, equipment, household domestic dwellings and refuse and solid waste sites. It is unknown how these sites are utilized by foraging bees or storage of colonies, so there is uncertainty regarding the potential for exposure through pollen and nectar. Furthermore, the fate characteristics of indoxacarb, and pattern of application method versus target pest (e.g., foliar application for foliar pests, no soil application for foliar pests) suggests that parent indoxacarb is not likely a systemic compound, and thus the exposures estimated with BeeRex may be overestimating potential

[10] http://www.ree.usda.gov/ree/news/Attractiveness_of_Agriculture_crops_to_pollinating_bees_Report-FINAL.pdf

residues in pollen and nectar.

Table 68. Summary of Tier I honeybee RQs for Oral Exposure Resulting from Foliar Uses of Indoxacarb

Use Pattern	Max Single Application Rate (lbs a.i./A)	Bee Life Stage	Dose (ug a.i./bee per 1 lbs a.i./A)	Indoxacarb Oral Dose (ug a.i./bee)	Acute RQ	Chronic RQ
Agricultural Uses-Foliar Spray						
-Group 15 Cereal Grains (sweet corn) -Group 18-10 Fruiting vegetable group -Subgroup 18C (Okra) -Crop Group 4. Leafy Vegetables (Except Brassica Vegetables): -Mint/peppermint/spearmint -Crop Group 5 (Brassica Leafy Vegetables): -Crop Sub-groups 5A & 5-B.	0.06525	Adult	32	2.09	**10.28**	N/A
	0.06525	Larvae	13.6	0.88	0.05	**52.81**
-Group 20 Oilseed group Subgroup 20C-Cotton -Crop Group 6 Legume Vegetables (succulent or dried) -6C (Dry succulent, except soybeans) -6A Edible-podded legume vegetables subgroup (soybeans) -Group 18 Nongrass animal feeds (forage, fodder, straw and hay) -Subgroup A (alfalfa) -Crop Group 9 (Cucurbit Vegetables): -Group 13-07 Berry and Small Fruit Subgroups 13-07D small vine climbing subgroup (except fuzzy kiwi) -13-07A Cranberry subgroup -13-07F Grapes -Peanuts -Crop Group 11 (Pome Fruits) -Crop Group 12 (Stone Fruits) -Crop Subgroup 12-12-B	0.1125	Adult	32	3.61	**17.72**	N/A
	0.1125	Larvae	13.6	1.53	0.08	**91.04**

-Crop Group 1. Root and Tuber Vegetables: -Subgroups 1A Beets -1C: Potato -Crop Group 4. Leafy Vegetables (Except Brassica Vegetables):						
Non-Agricultural Uses-Foliar Spray						
Commercial/institution/ industrial premises and equipment, recreational areas, households domestic dwellings non-agricultural uncultivated areas/soils and golf course turf	0.0375	Adult	32	1.20	**5.91**	N/A
		Larvae	13.6	19.5	0.03	**30.35**
Commercial/institutional/ industrial premises, equipment, household domestic dwellings and refuse and solid waste sites	1.437	Adult	32	46.15	**226.3**	N/A
		Larvae	13.6	19.5	**1.08**	**1162.9**
Non-Agricultural Soil Application						
Commercial/institution/ Industrial premises and equipment, recreational areas, households domestic dwellings non-agricultural uncultivated areas/soils and golf course turf	0.0375	Adult	32	1.20	0.04	N/A
		Larvae	13.6	0.51	0.00	0.20
Commercial/institutional/ industrial premises, equipment, household domestic dwellings and refuse and solid waste sites	1.437	Adult	32	46.15	**1.46**	N/A
		Larvae	13.6	19.5	0.01	**7.49**

Tier I RQs Agricultural and non-Agricultural Uses-Contact Exposure

Table 69 summarizes the acute contact RQ values for adult honey bees that are assumed to be foraging on treated crop during pesticide application. As the Tier I for acute contact exposure utilizes the maximum single application rate and a standard contact dose rate of 2.7 µg a.i./bee per 1 lbs. a.i./A, registered use patterns with the same maximum single application rate are grouped together. For all foliar uses assessed, adult acute contact RQ values range from 1.489-57.05 and all exceed the agency's LOC.

Table 69. Summary of Tier I honeybee RQs for Contact Exposure Resulting from Foliar Uses of Indoxacarb

Use Pattern	Max Single Application Rate (lbs ai/A)	Bee Life Stage	Dose (ug ai/bee per 1 lbs ai/A)	Contact Dose (ug ai/bee)	Acute Contact RQ
Agricultural Uses-Foliar Spray					
-Group 15 Cereal Grains (sweet corn) -Group 18-10 Fruiting vegetable group -Subgroup 18C (Okra) -Crop Group 4. Leafy Vegetables (Except Brassica Vegetables): -Mint/peppermint/spearmint -Crop Group 5 (Brassica Leafy Vegetables): -Crop Sub-groups 5A & 5-B.	0.06525	Adult	2.7	0.176	**2.59**
-Group 20 Oilseed group Subgroup 20C-Cotton -Crop Group 6 Legume Vegetables (succulent or dried) -6C (Dry succulent, except soybeans) -6A Edible-podded legume vegetables subgroup (soybeans) -Group 18 Nongrass animal feeds (forage, fodder, straw and hay) -Subgroup A (alfalfa) -Crop Group 9 (Cucurbit Vegetables): -Group 13-07 Berry and Small Fruit Subgroups 13-07D small vine climbing subgroup (except fuzzy kiwi) -13-07A Cranberry subgroup -13-07F Grapes -Peanuts -Crop Group 11 (Pome Fruits) -Crop Group 12 (Stone Fruits) -Crop Subgroup 12-12-B -Crop Group 1. Root and Tuber Vegetables: -Subgroups 1A Beets -1C: Potato -Crop Group 4. Leafy Vegetables (Except Brassica	0.1125	Adult	2.7	0.304	**4.46**

Vegetables)					
Non-Agricultural Uses-Foliar Spray					
Commercial/institution/ industrial premises and equipment, recreational areas, households domestic dwellings non-agricultural uncultivated areas/soils and golf course turf	0.0375	Adult	2.7	0.101	**1.489**
Commercial/institutional/ industrial premises, equipment, household domestic dwellings and refuse and solid waste sites	1.437	Adult	2.7	**3.87**	**57.05**

Quantitative residue data are not available to refine Tier I RQs. When considering the available toxicity endpoints, a concentration <0.044 mg a.i./kg-food would pose a low risk for honey bees.

Comparsions between the BeeRex estimated acute and chronic dietary EECs for foliar application of 0.06525 lbs a.i./A (low agriculutural rate) to the available Tier II colony feeding studies suggests that residues are above the tested concentraions. As mentioned in the discussion of those studies above, the reliability of the studies for conclusive determination of colony level effects is low. Additional studies would need to be conducted to confirm that the current application rates do not result in colony level effects. Similarly, for the available semi-field tunnel studies, the application rates were below the labeled field rates for indoxacarb. The uncertainties resulting from inadequate study designs for determining a NOAEC and LOAEC for the current labeled rates leaves question to whether or not there are colony level risks resulting from the use of indoxacarb. However, the review of the available incident reports shows that for colonies that are in or proximate to the application site, colony level effects have been observed in cotton.

6.4 Risk Concerns to Terrestrial Plants

Agricultural Risk

For terrestrial plants, risk was modeled for a single application at 0.06525 lb ai/acre and 0.1125 lb ai/acre for broadcast liquid, spray chemigation, granular and aerial drift fraction forms. The LOC (1.0) was not exceeded for listed species. RQs were not calculated for non-listed species because the EC_{25} was non-definitive (no effects at the highest test concentration). Since there is not a risk concern for listed species there is not a risk concern for non-listed species.

Non-Agricultural Risk

For non-agricultural indoxacarb uses, the risk to terrestrial plants was modeled at the lowest application rate of 0.0375 lbs ai/acre and the maximum application rate of 1.437 lbs ai/acre for broadcast liquid. The maximum tested rate in the terrestrial plant studies was 0.11 lbs ai/acre, which is less than the maximum non-agriculural application rate. No effects on terrestrial plants were indicated in these studies, and any potential for adverse effects between the maximum test dose and the maximum application rate (1.43 lbs ai/acre), remain uncertain.

7.0 Risk to Listed Species

Consistent with EPA's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to federally listed threatened and endangered (listed) species from registered uses of pesticides in accordance with the Joint Interim Approaches developed to implement the recommendations of the April 2013 National Academy of Sciences (NAS) report, *Assessing Risks to Endangered and Threatened Species from Pesticides*. The NAS report outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA. EPA will address concerns specific to indoxacarb in connection with the development of its final registration review decision for indoxacarb.

In November 2013, EPA, the U.S. Fish and Wildlife Service, National Marine Fisheries (the Services), and USDA released a white paper containing a summary of their joint Interim Approaches for assessing risks to listed species from pesticides. These Interim Approaches were developed jointly by the agencies in response to the NAS recommendations, and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. Details of the joint Interim Approaches are contained in the November 1, 2013 white paper, *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report.*

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, this ecological problem formulation supporting the Preliminary Work Plan for indoxacarb does not describe the specific ESA analysis, including effects determinations for specific listed species or designated critical habitat, to be conducted during registration review. While the agencies continue to develop a common method for ESA analysis, the planned risk assessment for the registration review of indoxacarb will describe the level of ESA analysis completed for this particular registration review case. This assessment will allow EPA to focus its future evaluations on the types of species where the potential for effects exists, once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methods necessary to complete risk assessments for listed species and their designated critical habitats, these methods will be applied to subsequent analyses of indoxacarb as part of completing this registration review.

8.0 Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of registration review for indoxacarb, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), indoxacarb is not subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a “naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 20138F[11] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.
Indoxacarb is not on the first or second list chemicals for which EPA intends to issue test orders/data call-ins in the near future. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit the website, http://www.epa.gov/endo/.

9.0 Risk Conclusions

This assessment concludes that there are few mammalian acute risk concerns; however, there are chronic effects concerns across all application rates modeled. For birds, there are acute risk concerns at all agricultural and non-agricultural application rates, but only chronic risk concerns at the greatest non-agricultural application rate for perimeter uses at commercial/industrial sites and at households/domestic dwellings. There were only acute bioaccumulation concerns for sandpipers consuming contaminated fish. Both acute and chronic risk concerns were identified to pollinators, however, the Tier II qualitative field studies were conducted below field rates and indicate mixed colony responses, therefore no conclusion on the impacts to colonies can be made at this time. However, several highly pollinator attractive crops are registered for indoxacarb use and there was an incident involving a honeybee hive die-off on a cotton field. These lines of evidence suggest that there may be risks to honeybee colonies. There are chronic risk concerns for all uses for benthic invertebrates, and several uses have single season exceedances for water column invertebrates that can be estimated with a high confidence of risk. There is a high confidence of low risk potential for fish, terrestrial plants and aquatic plants.

[11] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

10.0 References

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Appendix A. Submitted Studies Cited in the Risk Assessment

Effects Studies

MRID	Citation Reference
44477113	Sarver, J. (1996) Acute Oral Toxicity Study with DPX-MP062 Technical (Approximately 75% DPX-KN128, 25% DPX-KN127) in Male and Female Rats: Lab Project Number: 10581-001: HLR 910-96: 910-96. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 56 p.
44477115	Kern, T. (1997) Acute Oral Toxicity Study with DPX-KN128 Technical in Male and Female Rats: Final Report: Lab Project Number: 10720-001: HLO-1997-00055: WIL-189093. Unpublished study prepared by WIL Research Labs., Inc. 123 p.
44477116	Kern, T. (1997) Acute Oral Toxicity Study with IN-KG433 Technical in Male and Female Rats: Final Report: Lab Project Number: 11202-001: HLO-1997-00469: WIL-189109. Unpublished study prepared by WIL Research Labs., Inc. 81 p.
44477117	Sarver, J. (1996) Acute Oral Toxicity Study with IN-JT333 in Male and Female Rats: Final Report: Lab Project Number: 10578-001: 927-96: HLR 927-96. Unpublished study prepared by WIL Research Labs., Inc. 68 p.
44477129	MacKenzie, S. (1997) Subchronic Oral Toxicity: 90-Day Study with DPX-MP062 (Approximately 75% DPX-KN128, 25% DPX-KN127) Feeding Study in Rats: Revision No. 1: Lab Project Number: 10668-001: DUPONT HL-1997-00056. Unpublished study prepared by Haskell Lab. for Toxicology and Industrial Medicine. 462 p.
44477132	Malek, D. (1997) Subchronic Oral Toxicity: 90-Day Study with DPX-JW062-69 (99.7% DPX-KN128) Feeding Study in Rats: Revision No. 1: Lab Project Number: 9793-001: DUPONT HLR 301-94: 301-94. Unpublished study prepared by Haskell Lab. for Toxicology and Industrial Medicine. 552 p.
44477139	Munley, S. (1997) Developmental Toxicity Study of DPX-JW062-106 in Rats: Revision No. 1: Lab Project Number: 9961-001: DUPONT HLR 558-95: 558-95. Unpublished study prepared by Haskell Lab. for Toxicology and Industrial Medicine. 206 p.
44477201	Palmer, S.; Grimes, J.; Beavers, J. (1997) DPX-MP062 Technical (Approximately 75% DPX-KN128, 25% DPX-KN127): An Acute Oral Toxicity Study With the Northern Bobwhite: Amended Report: Lab Project Number: AMR 3940-96: 112-432: 112/042996/QLD.NC/SUB112. Unpublished study prepared by Wildlife International Ltd. 59 p.
44477202	Campbell, S.; Beavers, J. (1997) DPX-JW062-83: An Acute Oral Toxicity Study With the Mallard: Lab Project Number: HLO# 691-94: 112-402: 691-94. Unpublished study prepared by Wildlife Internati.0onal Ltd. 28 p.
44477203	Palmer, S.; Beavers, J. (1997) IN-JT333-20: An Acute Oral Toxicity Study With the Northern Bobwhite: Lab Project Number: 112-431: 3890-96: 112/031996/QLD.NC/SUB112. Unpublished study prepared by Wildlife International Ltd. 47 p.

44477204 Palmer, S.; Beavers, J.; Grimes, J. (1997) DPX-MP062 Technical (Approximately 75% DPX-KN128, 25% DPX-KN127): A Dietary LC50 Study With the Mallard: Amended Report: Lab Project Number: AMR 4093-96: 112-438: 112/073096/MLCSDT.WC/SUB112. Unpublished study prepared by Wildlife International Ltd. 49 p.

44477205 Frey, L.; Beavers, J.; Jaber, M. (1997) DPX-MP062 Technical (Approximately 75% DPX-KN128, 25% DPX-KN127): A Reproduction Study With the Northern Bobwhite (Colinus virginianus): Amended Report: Lab Project Number: AMR 4096-96: 112-441: 112/073096/QR.WC/SUB112. Unpublished study prepared by Wildlife International Ltd. 210 p.

44477206 Frey, L.; Beavers, J.; Jaber, M. (1997) DPX-MP062 Technical (Approximately 75% DPX-KN128, 25% DPX-KN127): A Reproduction Study With the Mallard (Anas platyrhynchos): Amended Report: Lab Project Number: AMR 4095-96: 112-442: 11018. Unpublished study prepared by Wildlife International Ltd. 206 p.

44477208 Beavers, J.; Gallagher, S.; Stence, M. et al. (1996) DPX-JW062-106: A Reproduction Study With the Mallard (Anas platyrhynchos): Lab Project Number: 112-409: AMR 3215-94: HA-95-057. Unpublished study prepared by Wildlife International Ltd., 170 p.

44477209 Hoke, R. (1997) DPX-MP062 (Approximately 75% DPX-Kn128, 25% IN-KN127): Flow-through, Acute, 96-Hour LC50 to Rainbow Trout, Oncorhynchus mykiss: Revision No. 2: Lab Project Number: 911-96: 10769-001. Unpublished study prepared by E. I. du Pont de Nemours & Company. 39 p.

44477210 Hoke, R. (1997) DPX-MP062 (Approximately 75% DPX-KN128, 25% IN-KN127): Flow-through, Acute, 96-Hour LC50 to Bluegill Sunfish, Lepomis macrochirus: Revision No. 2: Lab Project Number: 912-96: 10769-001. Unpublished study prepared by E. I. du Pont de Nemours & Company. 37 p.

44477211 Hoke, R. (1997) DPX-MP062 (Approximately 75% DPX-KN128, 25% IN-KN127): Flow-through, Acute, 96-Hour LC50 to Channel Catfish, Ictalurus punctatus: Revision No. 2: Lab Project Number: 866-96: 10769-001. Unpublished study prepared by E. I. du Pont de Nemours & Company. 36 p.

44477212 Brown, M. (1997) DPX-JW062-106 (Racemic Mixture of DPX-KN128 and DPX-KN127): Flow-through, Acute, 96-Hour LC50 to Carp, Cyrinus carpio: Lab Project Number: 879-96: 10125. Unpublished study prepared by E.I. du Pont de Nemours & Company. 44 p.

44477213 Grube, P. (1997) DPX-MP062 150SC: Static-Renewal, Acute, 96-Hour LC50 to Rainbow Trout, Oncorhynchus mykiss: Lab Project Number: HL-1997-00654: 10721. Unpublished study prepared by E. I. du Pont de Nemours & Company. 35 p.

44477214 Kreamer, G. (1997) DPX-MP062 30WG: Static-Renewal, Acute, 96-Hour LC50 to Bluegill Sunfish, Lepomis macrochirus: Lab Project Number: HL-1997-00025: 11374. Unpublished study prepared by E. I. du Pont de Nemours & Company. 36 p.

44477215 Kreamer, G. (1997) DPX-MP062 30WG: Static-Renewal, Acute, 96-Hour LC50 to Rianbow Trout, Oncorhynachus mykiss: Lab Project Number: HL-1997-00508: 11374. Unpublished study prepared by E. I. du Pont de Nemours & Company. 35 p.

44477216 Hoke, R. (1997) IN-JT333-20: Flow-through, Acute, 96-Hour LC50 to Rainbow Trout, Oncorhynchus mykiss: Lab Project Number: HL-1997-00180: 10584. Unpublished study prepared by E. I. du Pont de Nemours & Company. 33 p.

44477217 Hoke, R. (1997) IN-KG433 Technical: Flow-through, Acute, 96-Hour Limit Test to Rainbow Trout, Oncorhynchus mykiss: Lab Project Number: HL-1997-00412: 11326. Unpublished study prepared by E. I. du Pont de Nemours & Company. 31 p.

44477218 Hoke, R. (1997) IN-KN127 Technical: Flow-through, Acute, 96-Hour LC50 to Rainbow Trout, Oncorhynchus mykiss: Lab Project Number: HLR 990-96: 11019. Unpublished study prepared by E. I. du Pont de Nemours & Company. 34 p.

44477219 Hoke, R. (1997) DPX-MP062 (Approximately 75% DPX-KN128, 25% IN-KN127): Static, Acute, 48-Hour EC50 to Daphnia magna: Revision No. 2: Lab Project Number: HLR 603-96: 10769-001: Unpublished study prepared by E. I. du Pont de Nemours & Company. 34 p.

44477220 Grube, P. (1997) DPX-MP062 (Approximately 75% DPX-KN128, 25% IN-KN127): 10-Day, Spiked-Sediment Toxicity to the Midge, Chironomus tentans: Lab Project Number: HL-1997-01011: MR-5659: 970023. Unpublished study prepared by E. I. du Pont de Nemours & Company. 100 p.

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44477222 Boeri, R.; Magazu, J.; Ward, T. (1997) Flow-Through Acute Toxicity of DPX-MP062 to the Sheepshead Minnow, Cyprinodon variegatus: Revision No. 1: Lab Project Number: HLO-1997-00090: 802-DU: HA-96-064. Unpublished study prepared by T.R. Wilbury Labs., Inc. 58 p.

44477223 Boeri, R.; Magazu, J.; Ward, T. (1997) Flow-Through Acute Toxicity of DPX-MP062 to the Mysid, Mysidopsis bahia: Revision No. 1: Lab Project Number: HLO-1997-00205: 803-DU: 10769. Unpublished study prepared by T.R. Wilbury Labs., Inc. 57 p.

44477224 Boeri, R.; Magazu, J.; Ward, T. (1997) Acute Flow-Through Mollusc Shell Deposition Test With DPX-MP062: Revision No. 1: Lab Project Number: HLO-1997-00350: 10769: 10586. Unpublished study prepared by T.R. Wilbury Labs., Inc. 59 p.

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44477230 Sloman, T.; Leva, S. (1997) DPX-MP062 (Consisting of 75% DPX-KN128 and 25% DPN-KN127): Influence on Growth and Reproduction of Lemna gibba G3: Revision #1: Lab Project Number: AMR 3602-95: MR 10616. Unpublished study prepared by E. I. du Pont de Nemours & Company. 38 p.

44477231 Hughes, J.; Williams, T.; Conder, L. (1997) DPX-MP062-51A (Approximately 75% DPX-KN128, 25% DPN-KN127): Influence on Growth and Reproduction of Skeletonema costatum (Revision 2): (Final Report): Lab Project Number: 3771-96: 19-04-3: HA-96-064. Unpublished study prepared by Carolina Ecotox, Inc. 99 p.

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44477234 Palmer, S.; Beavers, J. (1994) DPX-JW062-47: An Acute Contact Toxicity Study With the Honey Bee: Final Report: Lab Project Number: 112-361: 277-94: 9699-001. Unpublished study prepared by Wildlife International Ltd. 17 p.

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44477236 Palmer, S.; Beavers, J.; Priester, T. (1997) DPX-MP062-58 30 WG Formulation Containing 30% (W/W) DPX-KN128: Honey Bee Toxicity of Residues on Alfalfa Foliage: Revision No. 1: Amended Report: Lab Project Number: AMR 3866-96: 112-435. Unpublished study prepared by Wildlife International Ltd. and McKenzie Labs., Inc. 98 p.

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Environmental Fate Studies

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Appendix B. Non-Agricultural Indoxacarb Uses

Table 1. Non-Agricultural Indoxacarb Use. All application method timing is as needed. **Bold =** Outdoor (or terrestrial) indoxacarb uses[1].

Product Name Registration Number	Uses	Maximum Application Rate	Application Method	Application Method Timing
Advion Insect Granule 100-1483	**Commercial/institutional/industrial premises/equipment (outdoor)** Household/domestic dwellings (indoor)	0.1101 lb a.i./a	Broadcast Granule	When needed
	Commercial/institutional/industrial Premises/equipment (outdoor) Household/domestic dwellings (indoor)	0.0000275 lb/ linear ft	Perimeter Granule	When needed
	Commercial/institutional/industrial Premises/equipment (outdoor) Household/domestic dwellings (indoor)	0.00055 lb a.i./bait station	Bait Treatment	When needed
	Commercial/institutional/industrial Premises/equipment (indoor) **Household domestic dwellings (outdoor)**	0.4407 lb a.i./a	Perimeter Granule	When needed
	Golf Course Turf (outdoor) **Ornamental Lawns and Turf (outdoor)**	0.44 lb a.i./a	Broadcast Granule	When needed
Advion Cockroach Gel Bait 100-1484	Commercial/institutional/industrial Premises/equipment (indoor) **Commercial/institutional/industrial Premises/equipment (outdoor)** Commercial Transportation Facilities-non-feed/non-food (indoor) Commercial Transportation Vehicles (all or unspecified) (indoor) Eating Establishments Food Serving Areas (indoor) Feed/Food storage areas-full (indoor) Food processing plant premises (indoor) Food stores/supermarkets premises (indoor) Hospitals/medical institutions premises (human/veterinary)	0.00000331 lb a.i./ft	Crack and crevice and/or spot treatment[2]	When needed.

Product Name Registration Number	Uses	Maximum Application Rate	Application Method	Application Method Timing
	Household/domestic dwellings (indoor) premises **Household domestic dwellings (outdoor)** **Refuse and solid waste sites (outdoor)** Zoos (indoor)			
Advion Gel Cockroach Bait Arena 100-1486	Commercial/institutional/industrial Premises/equipment (indoor) **Commercial/institutional/industrial Premises/equipment (outdoor)** Commercial Transportation Vehicles (all or unspecified) (indoor) Eating Establishments (indoor) Food processing plant premises (indoor) Household/domestic dwellings (indoor) **Household domestic dwellings (outdoor)**	0.00000219 lb a.i./ft	Bait Treatment	When needed
Adivon Ant Gel 100-1498	Commercial/institutional/industrial Premises/equipment (indoor) **Commercial/institutional/industrial Premises/equipment (outdoor)** Commercial Transportation Facilities-non-feed/non-food (indoor) Commercial Transportation Vehicles (all or unspecified) (indoor) Eating Establishments (indoor) Food stores/supermarkets premises (indoor) Hospitals/medical institutions premises (human/veterinary) (indoor) Household/domestic dwellings (indoor) **Household domestic dwellings (outdoor)** Refuse/solid waste sites (indoor)	Unspecified	Bait Treatment	When needed

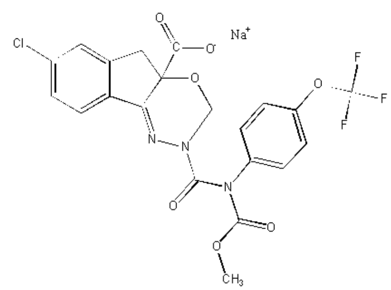
Product Name Registration Number	Uses	Maximum Application Rate	Application Method	Application Method Timing
	Zoos (indoor)			
	Commercial/institutional/industrial Premises/equipment (outdoor) Commercial Transportation Facilities-non-feed/non-food (indoor) Commercial Transportation Vehicles (all or unspecified) (indoor) Eating Establishments (indoor) Feed/Food storage areas-full (indoor) Food processing plant premises (indoor) Food stores/supermarkets premises (indoor) Hospitals/medical institutions premises (human/veterinary) (indoor) Household/domestic dwellings (indoor) **Household domestic dwellings (outdoor)** **Refuse/solid waste containers (garbage cans) (outdoor)** Refuse/solid waste sites (indoor) Zoos (indoor)	0.0000011 lb a.i./spot	Crack and Crevice and/or spot treatment[2]	When needed
Arilon 100-1501	Commercial/institutional/industrial Premises/equipment (indoor) Commercial Transportation Facilities-non-feed/nonfood (indoor) Commercial Transportation Vehicles (all or unspecified) (indoor) Eating Establishments (indoor) Feed/Food storage areas-full (indoor) Food processing plant equipment (indoor)	0.3593 lb a.i./a	Crack Crevice and/or spot treatment[2]	When Needed

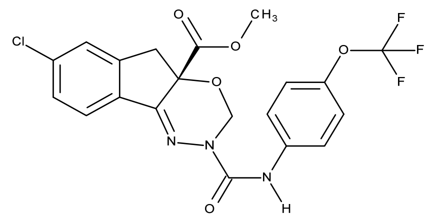
Product Name Registration Number	Uses	Maximum Application Rate	Application Method	Application Method Timing
	Food processing plant premises (indoor) Food stores/supermarkets premises (indoor) Hospitals/medical institutions premises (human/veterinary) (indoor) Households/domestic dwellings(indoor) Refuse/solid waste sites (indoor) **Refuse/solid waste sites (outdoor)** Zoos (indoor)			
	Commercial/institutional/industrial Premises/equipment (outdoor) **Household domestic dwellings (outdoor)**	0.179 lb a.i./a	High volume spray (dilute)	When needed
	Commercial/institutional/industrial Premises/equipment (outdoor) **Household domestic dwellings (outdoor)**	0.5389 lb a.i./a	High volume spray (dilute), Low volume spray (concentrate)	When needed
	Commercial/institutional/industrial Premises/equipment (outdoor) **Household domestic dwellings (outdoor)**	0.0165 lb a.i./mound	Mound treatment	When needed
	Commercial/institutional/industrial Premises/equipment (outdoor) **Household domestic dwellings (outdoor)**	1.437 lb a.i./a	Crack and crevice and/or spot treatment[2], Outdoor general surface spray, and perimeter.	When needed
Provaunt 100-1487	**Commercial/institutional/industrial Premises/equipment (outdoor)** **Golf Course Turf (outdoor)** **Household domestic dwellings (outdoor)** **Non-agricultural uncultivated areas/soils (outdoor)** **Recreational Areas (outdoor)**	0.03 lb a.i./a	Broadcast ground and sprayer	When needed
	Ornamental Lawns and Turf (outdoor)	0.225 lb a.i./a	Broadcast Sprayer	When needed
	Ornamentals Unspecified (outdoor)	0.225 lb a.i./ac	Foliar Treatment Sprayer	When needed

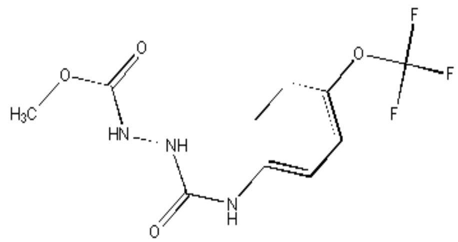
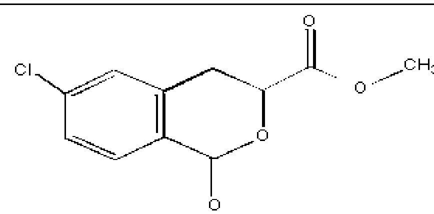
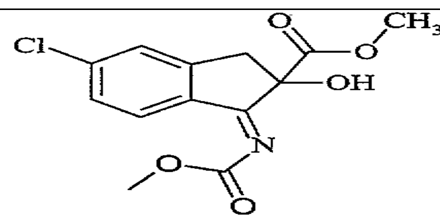
[1]Indoxacarb also has domestic animal uses (*i.e.,* spot treatment on cats)

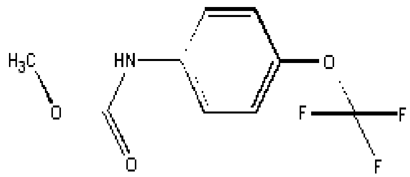
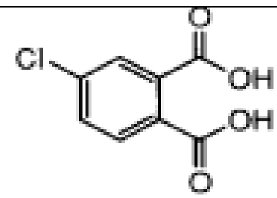
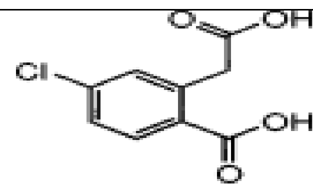
[2]Crack and Crevice use was not modeled and considered to have a low exposure potential for birds and mamamals.

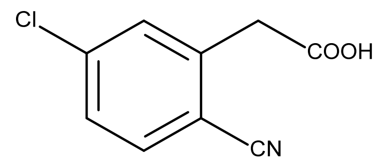
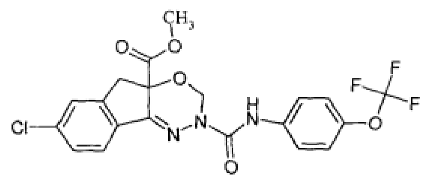
Appendix C. Indoxacarb Degradation Profile

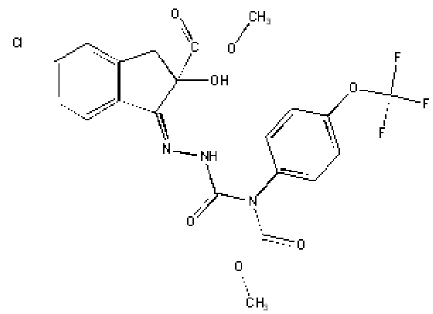
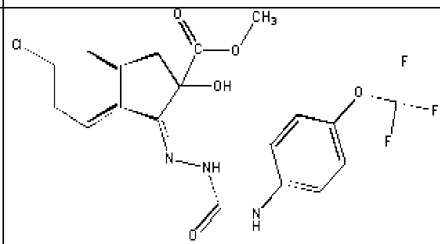
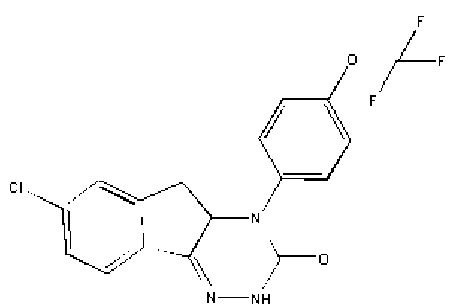
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-KT413	**CAS Name:** sodium 7-chloro-2,5,-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][l,3,4]oxadiazine-4a(3H)-carboxylic acid **Molecular Weight:** 513.82 g/mol (free acid) **SMILES**: COC(=O)N(c1ccc(cc1)OC(F)(F)F)C(=O)N2CO[C@]3(Cc4cc(ccc4C3=N2)Cl)C(=O)O.[Na+]		Hydrolysis	44477301	**48.0**
			Hydrolysis pH 7	49577705	**68.7**
			Hydrolysis pH 9	45795801	**88.1**
			Aerobic Aquatic Metabolism	45793301	**42.1**
			Aerobic Aquatic Metabolism	49577708	**83.0**
			Aerobic Soil Metabolism	49577707	**25.2**
			Anaerobic Aquatic Metabolism	44477305	**16.0**
			Terrestrial Field Dissipation	49577701	**19.6**
			Terrestrial Field Dissipation	49577702	**13.3**
			Terrestrial Field Dissipation	49577704	**12.7**

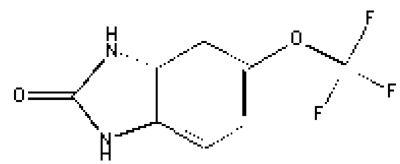
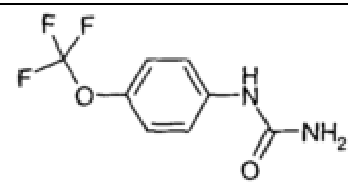
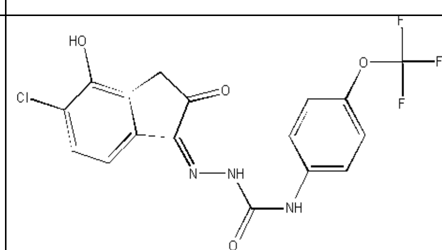
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-KN125 **(S-enantiomer of IN-JT333)**	**CAS Name:** Methyl (4aS)-7-chloro-2-[[4-(trifluoromethoxy)phenyl]carbamoyl]-3,5-dihydroindeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate **Formula:** $C_{20}H_{15}ClF_3N_3O_5$ **MW:** 469.8 g/mol **SMILES:** [H]N(c1ccc(cc1)OC(F)(F)F)C(=O)N2CO[C@]3(Cc4cc(ccc4C3=N2)Cl)C(=O)OC		Anaerobic Soil Metabolism	49577707	**10.6**
	CAS Name:		Hydrolysis pH 5	45795801	6.1

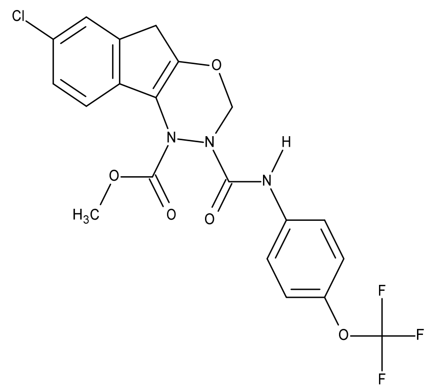
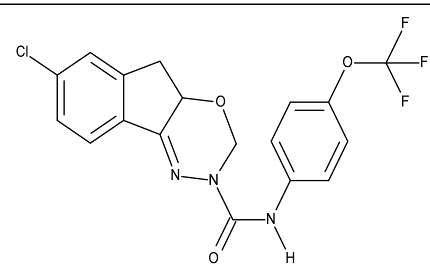
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-MF014	methyl 2-[[[4-(trifluoromethoxy)phenyl] amino]carbonyl]hydrazine carboxylate		Hydrolysis pH 7		**14.7**
			Aqueous Photolysis	44477302	**37.8**
			Aqueous Photolysis	45795802	**37.6**
IN-MH304	**CAS Name:** Not Reported		Aqueous Photolysis	44477302	**19.9**
			Aqueous Photolysis	45795802	**32.3**
MW 297	**CAS Name:** Not Reported	 Proposed structure; not proven due to inability to synthesize standard	Aqueous Photolysis	44477302	**14.1**
IN-KB687	**CAS Name:**		Aqueous Photolysis	44477302	**22.1**
			Aqueous Photolysis	45795802	**28.7**

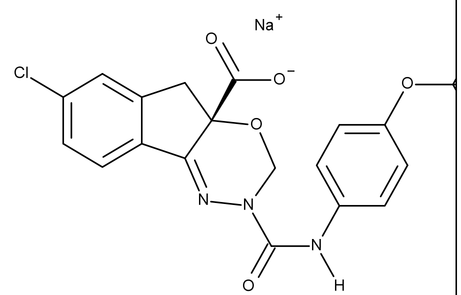
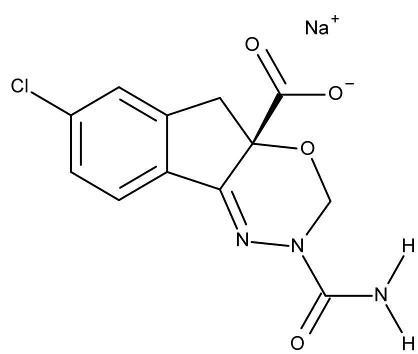
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
	methyl[4(trifluoromethoxy)phenyl]carbamate **Molecular Weight:** 235.16 g/mol		Soil Photolysis	44477303	**22.0**
			Aerobic Soil Metabolism	44477304	**11.0**
IN-C0639	**CAS Name:** 4-chloro-1,2-benzenedicarboxylic acid		Aqueous Photolysis	45795802	**10.2**
IN-MA573	**CAS Name:** 2-carboxy-5-chloro benzeneacetic acid		Aqueous Photolysis	45795802	**19.9**

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-U8F52	**CAS Name:** 2-(5-Chloro-2-cyano-phenyl)acetic acid **Formula:** $C_9H_6ClNO_2$ **MW:** 195.6 g/mol **SMILES:** c1cc(c(cc1Cl)CC(=O)O)C#N		Anaerobic Soil Metabolism	49577707	**14.7**
IN-JT333	**CAS Name:** methyl-7-chloro-2,5-dihydro -2-[[[4(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine -4a(3H)-carboxylate **Molecular Weight:** 469.81 g/mol		Aerobic Soil Metabolism	45906701	**18.6**
			Aerobic Aquatic Metabolism	44477306	**10.5**
			Aerobic Aquatic Metabolism	45793301	**25.7**
			Anaerobic Aquatic Metabolism	44477305	**28.2**

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-KG433	**CAS Name:** Methyl-5-chloro-2,3-dihydro-2-hydroxy-1[[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]hydrazono]-1H-indene-2-carboxylate **Molecular Weight:** 515.83 g/mol		Aerobic Soil Metabolism	45166303	**39.7**
IN-JU873	**CAS Name:** 1-[[[[4-(trifluoromethoxy)phenyl] amino] carbonyl]hydrazono]-1H-indene-2-carboxylate **Molecular Weight:** 457.8 g/mol		Aerobic Soil Metabolism	45166303	**12.9**
IN-ML438	**CAS Name:** 7-chloro-2,4-dihydro-4-[4-4 -(trifluoromethoxy)phenyl]-3H-indeno[2,1-e]-1,2,4-triazin-3-one **Molecular Weight:** 379 g/mol		Aerobic Soil Metabolism	45166303	**9.7**

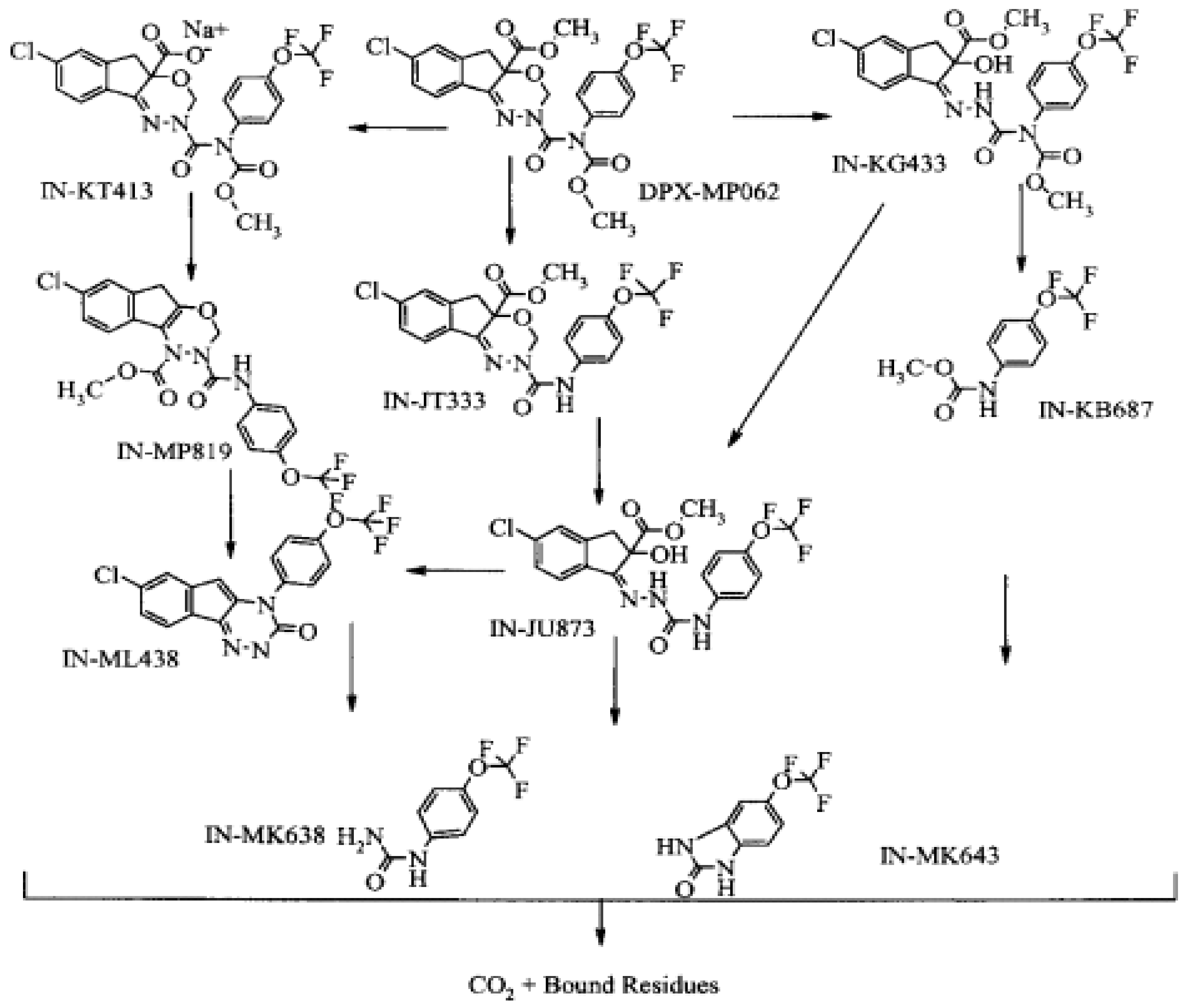
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-MK643	**CAS Name:** l,2-dihydro-5-(trifluoromethoxy)-2H-benzimidazol-2-one **Molecular Weight:** 218.14 g/mol		Aerobic Soil Metabolism	45166303 44477304	**12.0**
IN-MK638	**CAS Name:** [4-(Trifluoromethoxy)phenyl]urea **Formula**: $C_8H_7F_3N_2O_2$ **MW**: 220.1 g/mol **SMILES**: [H]N([H])C(=O)N([H])c1ccc(cc1)OC(F)(F)F		Aerobic Soil Metabolism	45166303	**28.1**
IN-ML437-OH	**CAS Name:** **Not Reported**		Aerobic Soil Metabolism	44477304	**13.0**

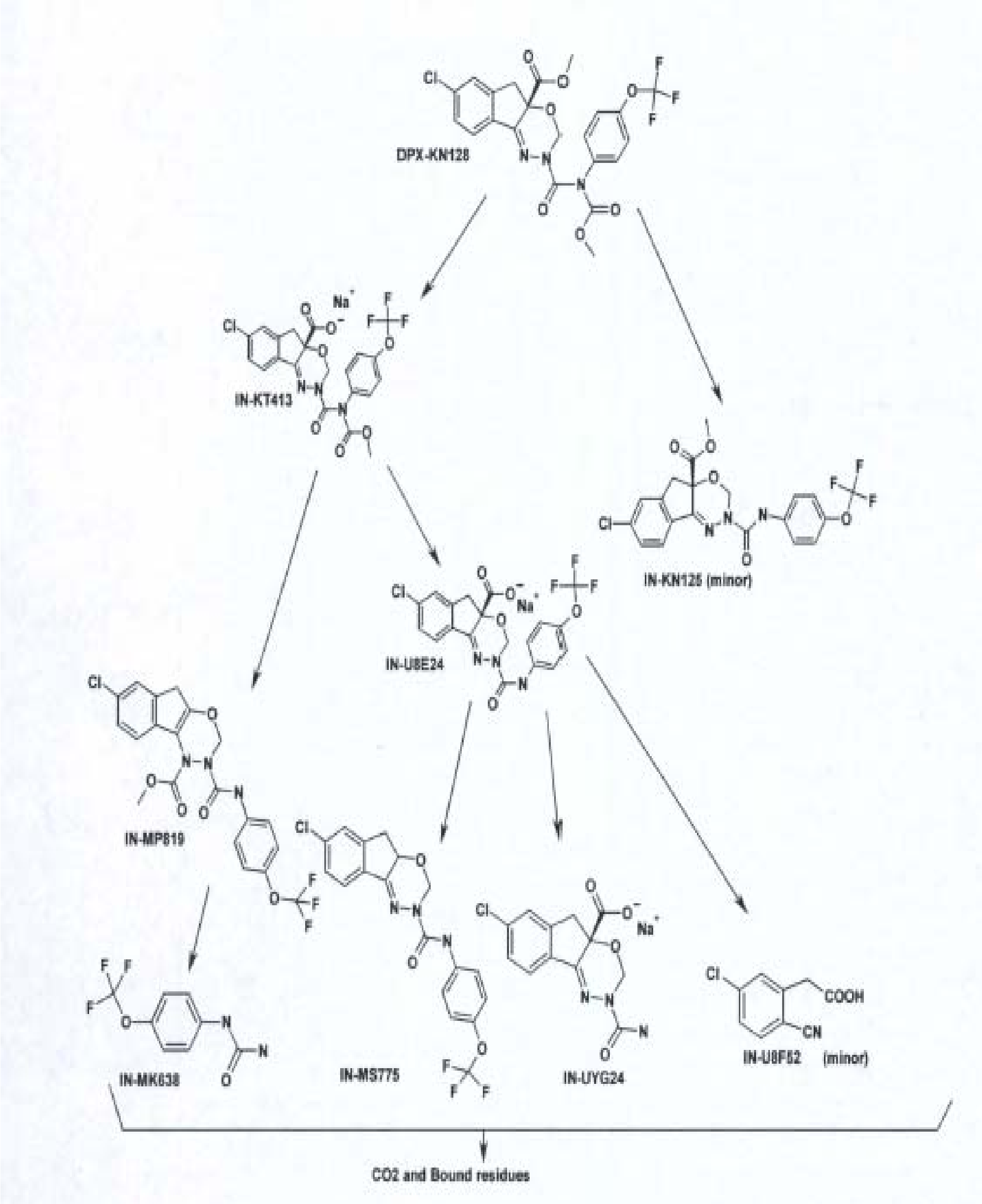
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-MP819	**CAS Name:** Indenol[1 ,2-e][1 ,3,4]oxadlazine-1 (2H)-carboxylic acid, 7-chloro-3,5-dlhydno-2-[[[4-(triftuoromethoxy)phenyl]amino]carbonyl]-, methyl ester **Formula**: $C_{20}H_{15}ClF_3N_3O_5$ **MW**: 469.8 g/mol **SMILES**: [H]N(c1ccc(cc1)OC(F)(F)F)C(=O)N2COC3=C(N2C(=O)OC)c4ccc(cc4C3)Cl		Hydrolysis	49577705	**12.4**
			Aerobic Aquatic Metabolism	45793301	**10.3**
			Aerobic Aquatic Metabolism	49577708	**21.3**
IN-MS775	**CAS Name:** 7-Chloro-N-[4-(trifluoromethoxy)phenyl]-4a,5-dihydro-3H-indeno[1,2-e][1,3,4]oxadiazine-2-carboxamide **Formula:** $C_{18}H_{13}ClF_3N_3O_3$ **MW:** 411.76 g/mol **SMILES:** [H]N(c1ccc(cc1)OC(F)(F)F)C(=O)N2COC3Cc4cc(ccc4C3=N2)Cl		Aerobic Aquatic Metabolism	45793301	**12.8**
			Anaerobic Soil Metabolism	49577707	**34.4**

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
IN-U8E24 **(S-enantiomer of IN-HVV36)**	**IUPAC:** Sodium;(4aS)-7-chloro-2-[[4(trifluoromethoxy)phenyl]carbamoyl]-3,5-dihydroindeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate **Formula:** $C_{19}H_{12}ClF_3N_3NaO_5$ **MW:** 477.75 g/mol **SMILES:** [H]N(c1ccc(cc1)OC(F)(F)F)C(=O)N2CO[C@]3(Cc4cc(ccc4C3=N2)Cl)C(=O)[O-].[Na+]		Aerobic Aquatic Metabolism	49577708	**24.3**
			Anaerobic Soil Metabolism	49577707	**40.0**
IN-UYG24 **(S-enantiomer of IN-UYG23)**	**IUPAC:** Sodium;(4aS)-2-carbamoyl-7-chloro-3,5-dihydroindeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate **Formula:** $C_{12}H_9ClN_3NaO_4$ **MW:** 317.66 g/mol **SMILES:** [H]N([H])C(=O)N1CO[C@]2(Cc3cc(ccc3C2=N1)Cl)C(=O)[O-].[Na+]		Aerobic Aquatic Metabolism	49577708	**31.6**
CO_2	**Carbon Dioxide**	O=C=O	Aerobic Soil Metabolism	45795803	**35.7**
			Aerobic Aquatic Metabolism	44477306	**19.0**

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum Formation (% Applied)
			Aerobic Aquatic Metabolism	45793301	**25.8**
Unextractable Residues			Aerobic Soil Metabolism	45906701	**66.1**
			Aerobic Aquatic Metabolism	49577708	**66.1**
			Anaerobic Soil Metabolism	49577707	**37.3**

Appendix D. Proposed Aerobic Soil and Aerobic Aquatic System Degradation Profile




DPX-KN128
IN-KT413
IN-KN125 (minor)
IN-U8E24
IN-MP819
IN-MK638
IN-MS775
IN-UYG24
IN-U8F52 (minor)
CO2 and Bound residues

Appendix E. T-Rex Input

Table 1. T-Rex Inputs and outputs for 0.06525 lb ai/Acre, 4 applications, 3-day interval and maximum application rate of 0.44 lbs a.i./Acre

% A.I.	100%
Application Rate	0.06525 lb ai/acre
Half Life	35 (days)
Application Interval	3 (days)
Number of Applications	1

Table 2. T-Rex Inputs and Outputs for 0.1125 lb ai/Acre, 4 applications, 3-day interval and maximum application rate of 0.44 lbs a.i./Acre

% A.I.	100%
Application Rate	0.1125 lb ai/acre
Half Life	35 (days)
Application Interval	3 (days)
Number of Applications	4

Table 3. T-Rex Inputs for 0.1125 lb ai/Acre, 4 applications, 5-day interval and maximum application rate of 0.44 lbs a.i./Acre

% A.I.	100%
Application Rate	0.1125 lb ai/acre
Half Life	35 (days)
Application Interval	5 (days)
Number of Applications	4

Table 4. T-Rex Inputs for 0.0375 lb ai/Acre, 12 applications, 7-day interval and maximum application rate of 0.45 lbs a.i./Acre

% A.I.	100%
Application Rate	0.0375 lb ai/acre
Half Life	35 (days)
Application Interval	7 (days)
Number of Applications	12

Table 5. T-Rex Inputs for 0.225 lb ai/Acre, 2 applications, 7-day interval and maximum application rate of 0.45 lbs a.i./Acre

% A.I.	100%
Application Rate	0.225 lb ai/acre
Half Life	35 (days)
Application Interval	7 (days)
Number of Applications	2

Table 6. T-Rex Inputs for 1.437 lb ai/Acre, 12 applications, 7-day interval and maximum application rate of 0.45 lbs a.i./Acre

% A.I.	100%
Application Rate	1.437 lb ai/acre
Half Life	35 (days)
Application Interval	7 (days)
Number of Applications	12