Title

Comparative Assessment of the Freshwater Aquatic Toxicity Profile for the Use of Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron-methyl For Railways

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EXECUTIVE OVERVIEW

In the following document, Bayer CropScience has compiled acute and chronic freshwater aquatic organism data, as defined by the U.S. EPA Environmental Fate and Effects Division (EFED) Screening Level Ecological Risk Assessments. These data are used in the following comparative risk assessment for freshwater aquatic organisms of four herbicides, Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron-methyl. Each of these active ingredients has an end use product with current registrations for use as non-crop, vegetation management.

Overall, risks to fish and aquatic invertebrates are low. No acute levels of concerns are exceeded in the reviewed use patterns for any of the herbicides investigated. Vegetation management use patterns also show low risk to algae; however, potential risk does exist for aquatic vascular plants exposed to low levels of herbicides. Duckweed, used as a conservative surrogate for aquatic vascular vegetation is sensitive when exposed to Indaziflam, Imazapyr, and Metsulfuron. For each of these herbicides, the U.S. EPA's level of concern is exceeded in this screening level risk assessment comparison. These findings are consistent with compounds that have herbicidal activity.

A.1. Risk Comparison of Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron-methyl

A.1.1 Use Patterns and Environmental Fate of Indaziflam, Aminocyclopyrachlor, Imazapyr and Metsulfuron-methyl

Table 1 provides a summary of application parameters and environmental fate data (from EPA, publically available sources) for Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron, presently registered for industrial vegetative management.

Table 1: Summary of Application Parameters and Environmental Fate Data

Application Information	Indaziflam	Aminocyclopyrachlor	Metsulfuron-methyl	Imazapyr
Product Label	Esplanade 200 SC ®	Streamline ®	Streamline ®	Polaris AC ®
Product Rate (railway)	5 fl oz	10 oz	10 oz	2 quarts
Application Rate (lb a.i./acre)	0.065	0.25	0.08	2.0
Chemical / Fate Property				
Molecular Weight (MW; g/mol)	301.4	213.6	381.4	293.2
Water Solubility (mg/L; pH 7, 25 °C)	2.8	2,810	109	11,100
Vapor Pressure (mm Hg)	1.9×10^{-10}, 20°C	3.7×10^{-8}, 25°C	2.5×10^{-12}	$<10^{-7}$, 60°C
Henry's Law Constant (H; atm•m^3/mol)	2.7×10^{-11}	3.47×10^{-12}	2.35×10^{-16}	$<7 \times 10^{-17}$
Octanol-Water Partition Coefficient (Log K_{ow})	631	-2.48	0.018	0.22
Sorption Partition Coefficient (L/kg; K_{oc})	496	9.8	155	19
Hydrolysis half-life (days)	stable	stable	stable	stable
Aqueous photolysis half-life (days)	3.7	7.8 (sterile) 1.4 (natural)	stable	2.5 – 5.3
Soil Photolysis half-life (days)	40	129	not available	149
Aerobic Soil Metabolism half-life (days)	68.0	224	36	>365
Anaerobic Soil Metabolism half-life (days)	stable	stable	not available	stable
Aerobic Aquatic Metabolism half-life (days)	179	stable	not available	stable
Anaerobic Aquatic Metabolism half-life (days)	stable	stable	35 - 365	stable

Indaziflam has a lower application rate (pounds active per acre) than the other herbicides, with the exception of metsulfuron-methyl, which is mixed with aminocyclopyrachlor, in the Streamline® product.

Indaziflam has the lowest mobility potential as indicated by it having the lowest water solubility, and highest sorption coefficient. All of the active ingredients are stable to hydrolysis (sterile conditions), but indaziflam, aminocyclopyrachlor and imazapyr will degrade well through photolysis in water (aqueous photolysis). Indaziflam will also be metabolized more readily than the other active ingredient on soil (aerobic soil metabolism) and in an aquatic environment (aerobic aquatic metabolism).

Considering the application rate and environmental parameters, indaziflam exhibits the best overall environmental exposure profile.

A.1.2 Risk Quotient Calculations

Risk characterization for indaziflam, aminocyclopyrachlor, imazapyr and metsulfuron-methyl, were performed for fish, aquatic invertebrates and aquatic plants using the basic methodologies described by U.S. EPA. Risk Quotients (RQs): (ratio of Estimated Environmental Concentration (EEC) and toxicity measurement endpoint) were used to characterize risk, and the final RQs compared to a Level of Concern (LOC) as a means to express potential concern for a taxonomic group or environmental entity. Additional consideration should be given to LOC exceedences in relationship to the conservative assumptions used in the risk assessment.

Screening level assessments were performed based on data obtained from the U.S. EPA's (the Agency) Ecological Risk Assessment documents, publically available, as prepared by the Office of Pesticide Programs. Screening level aquatic exposure assessments were preformed through generating highest baseline estimated environmental concentrations (EECs) based on the rates and applications as defined by the Industrial Vegetative Management (IVM) use patterns and labels for each herbicide product. These EECs were then compared to the lowest aquatic organism or plant endpoints generated from standard guideline studies to generate a risk quotient (RQ). Risk quotients were then compared to the U.S. EPA's defined levels of concern (LOCs). These LOCs are listed in Table 2 and Table 3. Peak EECs represent acute exposure, while 21-d EECs represent chronic exposure levels.

Throughout the discussions of ecological toxicity information presented in this document, the "quotient method" is used as a first characterization of the risk. For this method, risk quotients (RQ) are calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic.

The following relationship is used to calculate the risk quotient (RQ):

RQ = Exposure / Toxicity

Table 2: EPA Risk Presumption for Aquatic Animals

Risk Presumption for Aquatic Animals		
Risk Presumption	**Risk Quotient (RQ)**	**LOC**
Acute High Risk	EEC/LC_{50} or EC_{50}	0.5
Acute Restricted Use	EEC/LC_{50} or EC_{50}	0.1
Acute Endangered Species	EEC/LC_{50} or EC_{50}	0.05
Chronic Risk	EEC/NOEC or NOAEC[1]	1

[1]No Observed Adverse Effect Concentration

Table 3: EPA Risk Presumption for Plants

Risk Presumption for Aquatic Plants		
Risk Presumption	**Risk Quotient (RQ)**	**LOC**
Acute High Risk	EEC/EC_{50}	1
Acute Endangered Species	EEC/NOEC	1

[1]No Observed Adverse Effect Concentration

The risk quotients are then compared to EPA's Levels of Concern (LOC). These levels of concern are criteria used by the EPA to indicate potential risk to non-target organisms. Currently, LOCs address the following risk presumption categories:

1. **Acute High** – potential for acute risk is high and regulatory action may be warranted in addition to restricted use classification
2. **Acute Restricted Use** – the potential for acute risk is high, but this may be mitigated through restricted use classification
3. **Acute Endangered Species** – the potential for acute risk to endangered species is high and regulatory action may be warranted
4. **Chronic Risk** – the potential for chronic risk is high and regulatory action may be warranted.

A.1.3 Freshwater Aquatic Exposure Characterization

Screening level aquatic ecological exposure concentrations of indaziflam, aminocyclopyrachlor, imazapyr, and metsulfuron-methyl for the vegetative management uses were generated using the Tier I EPA screening model GENEEC. The screening EECs are presented in Table 4.

Table 4: Aquatic Ecological Estimated Concentrations (90th Percentile) Calculated Using GENEEC

Compound	IVM Seasonal Use Rate (lb a.i./A)	Estimated Environmental Concentration (µg/L)		
		Peak	21- Day	60- Day
Indaziflam	0.065	2.2	2.0	1.8
Aminocyclopyrachlor	0.247	14.6	13.8	12.2
Imazapyr	2.0	120.7	119.4	116.9
Metsulfuron	0.079	4.8	4.6	12.2

In the risk characterization for aquatic organisms, risk quotients (RQs) were calculated based on results of testing with technical grade active ingredient. In the Tier I exposure assessment,

EECs were chosen to match the duration of the toxicity tests for acute tests by using the peak exposure. For chronic exposure, 21 day EECs were used to assess risk. Using 21 day EECs for estimating chronic risk represent a conservative estimate, as that peak exposure and 21 day exposure levels did not vary drastically, and these EECs remained within 5 to 10% of each other. These peak and chronic level EECs represent a conservative risk approach

A.1.4 Freshwater Aquatic Risk Characterization

In the tables below, endpoints generated from standard toxicity tests with technical grade active ingredient are listed. The information given includes active ingredient, ecological endpoints, species, study report number, and study type. From the endpoints, the lowest acute and/or chronic ecotoxicological endpoint was selected for conservative RQs calculation as seen in bold. Any exceedences of LOCs, as defined in Table 2Table 3, are also bolded.

A.1.4.1 Fish (Aquatic Vertebrates)

Risks of indaziflam to aquatic organisms is relatively low, however, indaziflam is categorized by the Agency as “highly toxic” to freshwater fish on an acute exposure basis. This value is based on the toxicity endpoint only. Once potential exposure is considered, risk quotients for indaziflam fell below the Agency’s acute risk to non-listed species (Table 6). This is also the case for chronic exposure, representing listed species.

Table 5: Most sensitive Fish Acute and Chronic Toxicity of Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Active Ingredient	Test Organism	Study Type and Duration	Ecotoxicological Endpoint	Study Report MRID
Indaziflam	Bluegill sunfish	Acute, 96h Mortality	$LC_{50:}$ 0.32 mg a.i./L	47443233
	Fathead minnow	Chronic, Growth and Repro	NOAEC: 0.464 mg a.i./L	47443226
Aminocyclopyrachlor	Rainbow Trout	Acute, 96h, Mortality	$LC_{50:}$ 13 mg a.i./L	47560206
	Rainbow Trout	Chronic, Growth and Repro	NOAEC: 11 mg a.i./L	47560130
Imazapyr	Rainbow Trout	Acute, 96h, Mortality	LC_{50} >100 mg a.i./L	00131629
	Rainbow Trout	Chronic, Growth and Repro	NOAEC 43.1 mg a.i./L	41315804
Metsulfuron	Bluegill sunfish	Acute, 96h Mortality	LC_{50} >150 mg a.i./L	00125817
	Rainbow Trout	Chronic, Growth and Repro	NOAEC 4.5 mg a.i./L	44122801

Table 6: Acute & Chronic Toxicity Risk Quotients of Freshwater Fish: Comparison of IVM use Patterns for Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Acute Assessment Active Ingredient	96 h LC_{50} Rainbow Trout (mg a.i/L)	96 h LC_{50} Bluegill (mg a.i/L)	96 h LC_{50} Fathead Minnow (mg a.i/L)	Peak EEC (µg/L)	Freshwater RQ
Indaziflam	0.57	**0.32**	0.77	2.2	<0.01
Aminocyclopyrachlor	**13**	>120	n/a	14.6	<0.01
Imazapyr	**>100**	>100	>100[1]	120.7	<0.01
Metsulfuron	**>150**	>150	n/a	4.8	<0.01
Chronic Assessment Active Ingredient	**Rainbow Trout ELS NOEC (mg a.i/L)**	**Fathead Minnow ELS NOEC (mg a.i/L)**	**Fathead Minnow Life Cycle NOEC (mg a.i./L)**	**21 d EEC (µg/L)**	**Freshwater RQ**
Indaziflam	n/a	**0.464**	n/a	2.0	<0.01
Aminocyclopyrachlor	**11**	n/a	n/a	13.8	<0.01
Imazapyr	**43.1**	118	120	119.4	<0.01
Metsulfuron	**4.5**	n/a	n/a	4.6	<0.01

[1]Fathead minnow value n/a - Channel Catfish value listed as surrogate species; n/a = not available; bolded endpoints used in RQ calculation; bolded RQ values represent RQ exceedence

A.1.4.2 Freshwater Invertebrates

Endpoints for aquatic invertebrates are given below for each active ingredient. In each comparison, no LOCs were exceeded, indicating low risk for each of these compounds.

Table 7: Most sensitive Freshwater Invertebrates, Acute and Chronic Toxicity of Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Active Ingredient	Test Organism	Study Type and Duration	Ecotoxicological Endpoint	Study Report MRID
Active Ingredient Studies				
Indaziflam	Daphnia	Acute, 48h, Immobility	LC_{50}: >9.88 mg a.i./L	47443226
	Daphnia	Chronic, 21d, Reproduction	NOAEC: 0.340 mg a.i./L	47443235
Aminocyclopyrachlor	Daphnia	Acute, 48h, Immobility	LC_{50}: 39.7 mg a.i./L	47560126
	Daphnia	Chronic, 21d, Reproduction	NOAEC: n/a LOAEC: 0.37 mg a.i./L	47560129
Imazapyr	Daphnia	Acute, 48h, Immobility	LC_{50}: >100 mg a.i./L	00131632
	Daphnia	Chronic, 21d, Reproduction	NOAEC: 97.1 mg a.i./L	41315805
Metsulfuron	Daphnia	Acute, 48h, Immobility	LC_{50}: >150 mg a.i./L	00125817
	--	Chronic	NOAEC: n/a	--

n/a = not available

Table 8: Acute and Chronic Toxicity Risk Quotients of Freshwater Invertebrates: Comparison of IVM use Patterns for Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Acute Assessment Active Ingredient	48 h EC_{50} Daphnia magna (mg a.i/L)	Peak EEC (µg/L)	Freshwater RQ
Indaziflam	>9.88	2.2	<0.01
Aminocyclopyrachlor	39.7	14.6	<0.01
Imazapyr	>100	120.7	<0.01
Metsulfuron	>150	4.8	<0.01
Chronic Assessment Active Ingredient	**Daphnia 21d Reproduction NOEC (mg a.i/L)**	**21 d EEC (µg/L)**	**Freshwater RQ**
Indaziflam	0.340	2.0	<0.01
Aminocyclopyrachlor	0.37	13.8	0.04
Imazapyr	97.1	119.4	<0.01
Metsulfuron	n/a	4.6	n/a

n/a = not available; bolded values represent RQ exceedence

A.1.4.3 Aquatic Plants

In the screening level assessment for aquatic organisms, indaziflam only exceeded the Agency's LOCs for vascular aquatic plants. In Canada's PMRA assessments, indaziflam did not exceed the trigger value for fish, non-vascular aquatic plants, nor aquatic invertebrates. However, indaziflam did exceed the trigger values for duckweed. It is not unusual that duckweed may be sensitive to herbicidal treatments.

Higher tier studies with duckweed included exposing duckweed to indaziflam with sediment present in the test chamber. This exposure scenario represented more environmentally relevant exposure and showed a growth rate endpoint 5x less toxic than the standard guideline exposure. This indicates that more environmentally relevant exposure scenarios can substantially mitigate the toxicity to vascular aquatic plants.

In Canada, the PMRA required a one meter buffer for indaziflam to protect aquatic habitats. This buffer conclusion was reached based on a higher tier aquatic plant study performed, and PMRA determined that this small buffer would mitigate exposure risk, when non-handheld applications of indaziflam were made. The use of hand-held or backpack sprayer, spot treatment or inter-row hooded sprayers do not require buffer zones, nor do vegetative management uses of indaziflam.

Table 9: Most sensitive Vascular and Non-Vascular Aquatic Plants, Toxicity of Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Active Ingredient	Test Organism	Study Type and Duration	Ecotoxicological Endpoint	Study Report MRID
Indaziflam	Duckweed	Frond Number, 7d	EC_{50}: 0.000061 mg a.i./L	47743308
	Skeletonema[1]	Biomass, 96h	EC_{50}: 0.027 mg a.i./L	47443267
Aminocyclopyrachlor	Duckweed	Frond Number, 7d	EC_{50}: >122 mg a.i./L	47560134
	Anabaena	Biomass, 96h	EC_{50}: 7.4 mg a.i./L	47560201
Imazapyr*	Duckweed	Frond Number, 7d	EC_{50}: 0.024 mg a.i./L	40811802
	Anabaena	Cell Density	EC_{50}: 12.2 mg a.i./L	40811802
Metsulfuron	Duckweed	n/a	EC_{50}: 0.00036 mg a.i./L	41773902
	Green Algae	n/a	EC_{50}: 0.031 mg a.i./L	40639302

n/a = not available

[1] Skeletonema is a marine diatom; however, EFED used this endpoint to represent all aquatic nonvascular plants

*Isopropylamine Salt of Imazapyr is more toxic to aquatic vascular and non-vascular plants than Imazapyr acid, however, a sublethal endpoint, cell shape was used to define the lowest EC_{50} and has no environmental relevance based on the algae population. The NOEAC values are comparable, and duckweed was within a factor of 2 between the salt and acid forms.

Table 10: Acute Toxicity Risk Quotients of Aquatic Plants: Comparison of IVM use Patterns for Indaziflam, Aminocyclopyrachlor, Imazapyr, and Metsulfuron

Active Ingredient (mg a.i./L)	Duckweed EC_{50}	Pseudokirc. (FW Green Algae) EC_{50}	Anabaena (FW Cyano-bacteria) EC_{50}	Navicula (FW diatom) EC_{50}	Peak EEC (µg/L)	Non-vascular RQs	Vascular RQs
Indaziflam	**0.000061**	**0.074**	0.75	0.087	2.2	0.03	**36**
Aminocyclopyrachlor	**>122**	120	**7.4**	38	14.6	<0.01	<0.01
Imazapyr	**0.024**	71	**12.2**	41	120.7	<0.01	**5**
Metsulfuron	**0.00036**	**0.031**	n/a	n/a	4.8	0.15	**13.3**

n/a = not available; bolded endpoints used in RQ calculation; bolded RQ values represent RQ exceedence

A.2. Comparative Risk Conclusion

The data for all herbicide products were obtained from a number of sources, but primarily publicly available documents from regulatory agencies, such as EPA RED (Reregistration Eligibility Decision) and Registration Review documents.

The risk quotient determinations indicate that no acute LOCs were exceeded in fish, aquatic invertebrates, or aquatic non-vascular plants. Each herbicide, except aminocyclopyrachlor show potential exceedence of the LOC for vascular plants. However, this risk assessment is based on screening level exposures and toxicity determinations, which are conservative in nature.