Registration Decision RD2022-09

Tiafenacil, Tiafenacil 70WG Herbicide, Insight 339SC Herbicide

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Registration decision statement[1] for tiafenacil

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is granting registration for the sale and use of Tergeo Technical Herbicide, Tiafenacil 70WG Herbicide and Insight 339SC Herbicide (formerly called Tiafenacil 339SC Herbicide), containing the technical grade active ingredient tiafenacil, to control weeds in field corn, soybean, spring wheat, grapes, summerfallow and non-crop areas.

The Proposed Registration Decision PRD2022-01, *Tiafenacil, Tiafenacil 70WG Herbicide, Tiafenacil 339SC Herbicide,* containing the detailed evaluation of the information submitted in support of this registration, underwent a 45-day consultation period ending on 20 February 2022. The evaluation found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable. Health Canada received comments relating to the health, environmental and value assessments. The comments received during the consultation process as well as Health Canada's responses to these comments are summarized below. The final decision is consistent with the proposed registration decision.

Comments and responses

Comments on the dietary exposure assessment

Ecojustice and Friends of the Earth objected to the proposed registration of tiafenacil, as inclusion of the metabolite trifluoroacetic acid (TFA) along with the parent tiafenacil resulted in a dietary exposure estimate that was up to 102% of acceptable daily intake (ADI) for infants. The commenters noted that because the aggregate risk estimate from food and drinking water resulted in potential exposure to infants of up to 92% of the ADI for tiafenacil alone, cumulative exposure to other sources of the TFA metabolite could exceed the chronic risk for this metabolite in infants. In addition, the commenters did not agree with the use of conservative assumptions to justify any exceedance of the ADI. They also claimed that the uncertainty factor for vulnerable populations, such as infants, was reduced without explanation.

Health Canada response

Health Canada uses contemporary risk assessment methods that are based on sound science, are in accordance with the *Pest Control Products Act* (PCPA), Agency policies and practices, and are consistent with those of international pesticide regulatory partners.

As described in PRD2022-01 and included below, Health Canada applied uncertainty factors and determined target margins of exposure, including exposures to vulnerable populations, in a manner consistent with that described in the Science Policy Note SPN2008-01, *The Application of Uncertainty Factors and the PCPA Factor in the Human Health Risk Assessment of Pesticides*.

[1] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act.*

As explained in SPN2008-01 and PRD2022-01, the *Pest Control Products Act* requires the application of a 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data, which includes consideration of whether there is any evidence of sensitivity of the young, the seriousness of any relevant endpoints observed, and confidence in the database, among other aspects. Full details on how the PCPA factor is assessed are included in Section 4.0 of the SPN2008-01. In the case of tiafenacil, the explanation for reducing the PCPA factor was provided in Section 3.1.2, *Pest Control Products Act* hazard characterization, on page 15 of PRD2022-01.

It is important to note that all required studies that assess potential toxicity to infants and children were submitted for this technical active, and these studies followed OECD guidelines and Good Laboratory Practices.

In addition, while the lowest offspring NOAEL in the rat reproductive toxicity study was 2.6 mg/kg bw/day and the lowest developmental NOAEL was 20 mg/kg bw/day based on the rat developmental toxicity study, Health Canada used an even lower NOAEL of 0.35 mg/kg bw/day from the chronic rat study as the point of departure for determining the ADI. This NOAEL is 7.4-fold and 57-fold lower, respectively, than the level where there are **no** effects in offspring in reproductive or developmental studies.

Thus, although there was some evidence of effects in the young animal at higher dose levels, the reference values selected for risk assessment provide margins of greater than 700 to 5700 to the NOAELs determined in the young in reproductive and developmental toxicity studies, respectively, resulting in adequate protection of infants and children.

In calculating potential dietary exposure to tiafenacil, Health Canada made a number of highly conservative assumptions (described below) designed to ensure that dietary exposure is not underestimated for any segment of the population. For tiafenacil alone, dietary risks are not of concern, as the combined exposure from food and drinking water is up to a maximum of 92% of the ADI. As noted in the comment, when the metabolite TFA is included in the exposure assessment, the highest chronic exposure estimate is up to 101.5% of the ADI for one population sub-group. This risk assessment is referred to as a basic level (or first tier) assessment, meaning high-end or worst-case assumptions were applied. The outcome of the assessment does not indicate a chronic risk of concern for the following reasons:

- The ADI for tiafenacil is set at a level that is at least 100-fold less than the dose at which **no harmful effects** were observed in animals (in other words, the NOAEL), and more importantly, at least 700-fold lower than the dose at which **no** harmful effects were observed in the young in the reproduction and developmental toxicity studies.

- The estimated chronic exposure to infants overestimates the risk, as no refinements to the residue inputs were considered in the human health risk assessment. Some of the conservatisms used in the risk assessment are highlighted below:

- It was assumed that residues of tiafenacil were in or on every treated crop and animal commodity and would be at the limit of quantitation of the enforcement method of 0.01 ppm. However, most of the samples tested from the field trials had no detectable levels of residues.
- The conservative dietary inputs also assumed that residue levels persist at the same levels observed at the "farm gate". In other words, throughout storage, transport, food preparation to consumption, there would be no decline in residues over time. However, it is expected that, as is the case for most pesticide residues, tiafenacil residues, if present in or on foods, will decline over time with normal degradation during storage, transport and food preparation.
- It was also assumed that 100% of all crops for which the use of tiafenacil is approved will be treated every season or year and also, closest to the harvest time. This is extremely conservative and highly unlikely, based on the field application practices of pesticides.
- While TFA is one of the metabolites of tiafenacil, it is not the only source of TFA in the environment. TFA is also formed from natural sources, and therefore, in addition to being a common metabolite of several pesticides, industrial chemicals and pharmaceutical agents, it is also ubiquitous in the environment. Thus, as described below, using the assumption that TFA occurs as a result of tiafenacil alone also results in a significant overestimate of exposure and risk, and would therefore be protective:

    - Results from the confined accumulation studies in rotational crops were used for some of the food commodities. However, these studies were not conducted under realistic field conditions (in other words, conditions were exaggerated). For example, studies were conducted at threefold the maximum supported rate and, being in a confined environment, were protected from the weather elements with no potential for runoff or leaching.
    - Another source of information for inputs in the risk assessment was the European Union Market Basket Survey (MBS) for TFA (2017), which is also conservative in its estimates, as the results include the background level of TFA in soil from all sources, not just from tiafenacil.
    - Background levels of TFA in or on foods as a result of TFA already present in the environment were assumed to result from the use of tiafenacil, which is a highly conservative cumulative estimate.
    - EFSA (2014) performed a comprehensive dietary consumer exposure assessment from all sources of TFA when assessing the pesticide saflufenacil (a molecule related to tiafenacil). The sources of exposure taken into consideration in this assessment were TFA residues from primary and rotational crops using saflufenacil, TFA residues on those same crops from other pesticides that are metabolised to TFA, and other TFA residues in food resulting from environmental contaminants. No risks of concern were identified, which further supports the conclusion that pesticide and environmental sources of TFA do not present a risk to human health. Moreover, Health Canada's risk assessment considered TFA to be of equivalent toxicity to tiafenacil (ADI of 0.004 mg/kg bw/d) which is

conservative relative to the EFSA review, given EFSA used a higher ADI of 0.05 mg/kg bw/day for TFA in their assessment.

- A greater contribution of TFA comes from several non-pesticidal sources, and is also not of concern. This is further described in a study by Solomon et al., (2016) that investigated TFA and its natural and synthetic sources. The major synthetic source of TFA is from breakdown products of refrigerants such as hydrofluorocarbons (HFC) and hydrochlorofluorocarbons (HCFC). Although chemicals including pharmaceuticals, pesticides, and polymers are another synthetic source of TFA, the contribution of TFA from these sources is considered to be quite small in comparison. In addition, there is no way to discern from which source TFA originates, or to distinguish between pesticide and non-pesticide sources. The authors stated, "The conclusion is that current and estimated concentrations of TFA and its salts in the environment that result from degradation of HCFCs, HFCs and hydrofluoroolefin (HFOs) in the atmosphere do not present a risk to humans and environment. However, formation of TFA from the degradation of HCFCs and HFCs warrants continued attention, in part because of its long environmental lifetime."
- The Cumulative Assessment section of PRD2022-01 acknowledged that TFA is a metabolite of tiafenacil (metabolite M-32), and also noted that TFA is a common chemical that comes from many sources. In addition, it was noted that levels of TFA released into the environment from current agricultural uses in Canada, including tiafenacil, are generally minor compared to other sources. Nonetheless, Health Canada continues to monitor pesticide-related contributions of TFA to the environment, as well as any health-related information that becomes available for this degradate.

- Drinking water is the main contributor to the dietary exposure estimate for both tiafenacil and TFA for all subpopulations, particularly for infants. While the estimate for exposure from food alone was 14.7% of the ADI, food plus drinking water was up to 101.5% of the ADI. However, the estimated environmental concentrations (EECs) used to estimate the contribution from drinking water were calculated using conservative assumptions, and by design, will therefore overestimate the risks:

    - The EEC modelling for tiafenacil (which includes numerous environmental degradates including TFA) was modelled using a parent-daughter-granddaughter modelling approach. In this approach, chemicals are grouped together, and the most conservative fate properties of the grouped chemicals is used in the model. Hence, it overestimates the risk for the other chemicals included in the grouping.
    - A range of EECs were obtained for tiafenacil across different scenarios, each with regional soil and weather characteristics. The most conservative scenario and results were used in the risk assessment.

Therefore, on the basis of all the conservative inputs used in the dietary risk assessment, the chronic dietary risks for infants from exposure to tiafenacil and TFA are not of health concern.

Comments on the cumulative risk assessment

Ecojustice and Friends of the Earth stated that tiafenacil has a common mechanism of toxicity and mode of action (MOA) with other registered products, which would trigger a cumulative risk assessment of the several herbicides currently used in Canada that inhibit protoporphyrinogen IX oxidase (PPO).

Health Canada response

The Cumulative Assessment section of PRD2022-01 did note that tiafenacil belongs to the class of herbicides known as the PPO inhibitors, some of which share a common mechanism of toxicity. As part of the process in determining the need to conduct a cumulative risk assessment (CRA), other important considerations must be explored, such as defining and comparing the use patterns of the different chemicals belonging to a class of pesticides with a common mechanism of toxicity to determine if the same uses are registered, whether the uses are wide-ranging, if there are residential uses, and the potential for co-occurrence of exposure to the different chemicals. In addition, monitoring data from the Canadian Food Inspection Agency (CFIA) and/or the United States Department of Agriculture (USDA) Pesticide Data Program (PDP) are important sources of real-world data for dietary exposure, and are required in order to conduct a CRA.

Based on the available monitoring data collected over a decade *(>500,000 samples) for the currently registered eight PPO-inhibitor herbicides listed below in Table A*, it was concluded that **quantifiable residues are not expected** in treated crops, and for the vast majority of samples, **no detectable residues** were observed either. Only 0.024% of samples had residues above or equal to the limit of detection (LOD), but these were below the limit of quantification (LOQ), and well below the MRLs. Based on the residue data reviewed in support of the tiafenacil registration, as with the other PPO-inhibitors, quantifiable residues in treated crops, are also not expected. As such, no co-occurrence of quantifiable residues originating from any of the herbicides in the PPO-inhibitor group are expected on any crops, and thus the cumulative dietary risk assessment is acceptable.

Table A Summary of residue monitoring data by the Canadian Food Inspection Agency (CFIA, 2008–2017) and the USEPA Pesticide Data Program (PDP, 2010–2019) for PPO inhibitors for several food commodities

Pest control product	Data Source	# Samples tested	# Sample with residues greater than LOD[1]	% Positive	Residue range (ppm) in positive samples (greater than or equal to LOD)	LOD (ppm) range in different commodities
Carfentrazone-ethyl	CFIA	28 778	0	0%	NA	0.0009–0.009
	PDP	104 734	6	0.006%	0.002–0.015	0.001–0.03
Flumioxazin	CFIA	43	0	0%	NA	0.01
	PDP	59,068	7	0.012%	0.005–0.013	0.001–0.15

Pest control product	Data Source	# Samples tested	# Sample with residues greater than LOD[1]	% Positive	Residue range (ppm) in positive samples (greater than or equal to LOD)	LOD (ppm) range in different commodities
Saflufenacil	CFIA	No data	-	-	-	-
	PDP	49 484	2	0.004%	0.000005	0.000005–0.041
Sulfentrazone	CFIA	28 778	1	0.003%	0.005	0.001–0.009
	PDP	48 341	0	0%	NA	0.006–0.15
Fomesafen	CFIA	No data	-	-	-	-
	PDP	9477	0	0%	NA	0.005–0.03
Acifluorfen-sodium	CFIA	No data	-	-	-	-
	PDP	6195	0	0%	NA	0.05
Pyraflufen-ethyl	CFIA	28 778	1	0.003%	0.006	0.001–0.009
	PDP	31 795	0	0%	NA	0.001–0.03
Oxyfluorfen	CFIA	39 398	3	0.008%	0.003–0.008	0.0016–0.005
	PDP	75 389	105	0.139%	0.001–0.011	0.000007–0.2
Overall	Canada (CFIA)	125 775	5	0.004%		
	United States (PDP)	384 483	120	0.031%		
	Overall	**510 258**	**125**	**0.024%**		

[1] LOD = limit of detection. Residues are below the limit of quantification (LOQ).

In addition, there are no residential uses for the currently registered actives in this class. Only one of the actives is registered for use on golf course tees and greens, for which an aggregate risk assessment was not required. Accordingly, no significant residential (non-dietary) exposure is anticipated. As such, based on consideration of the available information as required under section 7(7)(b)(i) of the *Pest Control Products Act*, no cumulative health effects of concern have been identified for tiafenacil and other pest control products with a common mechanism of toxicity that would prevent the registration of tiafenacil, for which quantifiable residues in treated crops are also not expected.

The PMRA will continue to monitor the available information on this class of pesticides. If new information becomes available that indicates the need for a quantitative CRA, this will be conducted as a stand-alone evaluation, which is consistent with the process described in the PMRA's framework on cumulative health risk assessment (SPN2018-02).

Comments on the environmental risk assessment

Ecojustice and Friends of the Earth submitted a comment regarding exceedances of the level of concern (LOC) for aquatic plants, fish, aquatic-phase amphibians and algae, due to runoff. They pointed out that "no information is provided supporting the use of a 1 m spray drift buffer zone to mitigate these effects or to confirm that the PMRA has modelled outcomes with the buffer zone and confirmed that the LOC arising from runoff would no longer be exceeded". They stated that

the 1-meter buffer zone appears to be arbitrary, and that the PMRA does not have reasonable certainty that no harm will occur to these biota.

Health Canada response

When tiafenacil is used in accordance with label directions and the required precautions, the environmental risks associated with tiafenacil are acceptable.

There was a typographical error in a footnote in Table 25 of PRD2022-01. Table 25 is only applicable to the risk to aquatic organisms incurred through surface runoff. However, Footnote 2 of the table erroneously referred to the calculation of risk being from spray drift; it should state that it is for surface runoff.

Table 25 Further characterization of risk from to aquatic organisms exposed to tiafenacil from runoff

Organism class	Exposure	Uncertainty factor applied to endpoint	Endpoint value (mg a.i./L)	Runoff EEC[1] (mg a.i./L)	RQ[2]	LOC[3]	LOC exceeded
Freshwater species							
Fish	Chronic	NOEC (LDPH)[4]	0.00102	0.0039	**3.82**	1	**Yes**
Aquatic-phase amphibians	Chronic	NOEC	0.016	0.019	**1.19**	1	**Yes**
Vascular plants	Acute	EC_{50}/2	0.00287	0.0040	**1.39**	1	**Yes**
Algae	Acute	EC_{50}/2	0.0019	0.0040	**2.11**	1	**Yes**
Marine species							
Algae	Acute	EC_{50}/2	0.0029	0.0040	**1.38**	1	**Yes**

[1]EEC = Estimated Environmental Concentration. Calculated assuming a maximum application rate of 50 g a.i./ha to water bodies of 80 cm depth (fish) and 15 cm depth (amphibian).
[2]RQ = Risk quotient. The RQ is calculated by dividing the EEC from surface runoff by the endpoint value (RQ = EEC/endpoint value).
[3]LOC = Level of concern. The RQ is compared to the LOC.

Regardless of the attributes of the active ingredient, conditions may exist that could promote the runoff of any chemical (for example, steep slope, heavy rain). Runoff can occur both with compounds that are soluble in water (runoff with flow of water) or adsorbed to soil (soil-particle movement in runoff water). Both can enter aquatic systems in runoff and pose a risk to either free-swimming or sediment-dwelling organisms, respectively. As such, runoff advisory statements are required on all labels for outdoor uses, with the exception of products that are only registered for uses where a runoff statement would not be appropriate (for example, aquatic uses, uses in wood treatment facilities).

As indicated in PRD2022-01, a risk assessment was conducted for potential runoff of tiafenacil from the uses on fallow and field crops. Modelling was conducted for 28 different crop scenarios throughout Canada using the model Pesticide in Water Calculator (PWC) 1.52. The Canadian crop scenario that generated the maximum exposures resulting from surface runoff was used in the assessment of risk. The risk quotients (RQ) indicate a slight exceedance of the LOC (RQs =

1.2–3.8) which further supports the addition of the following runoff advisory statements on the labels:

> "*To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.*
>
> *Avoid application when heavy rain is forecast.*
>
> *Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative filter strip between the treated area and the edge of the water body.*"

Regarding spray drift and the associated spray buffer zones, the screening level risk assessment identified potential risk to aquatic organisms from direct overspray (Table 23 of PRD2022-01). Thus, further analyses were conducted to determine the size of spray buffer zone required to mitigate the potential effects of spray drift entering aquatic systems. The EECs in aquatic systems resulting from spray drift is determined using Health Canada's standard approach, a spray drift model for ground boom equipment. The model is based on spray drift trials, where the smallest off-target distance of spray drift measurement was 1 m (in other words, 1 m downwind from the edge of the field that was sprayed). Based on the spray drift model, which takes into account mode of application (ground boom sprayer) and American Society of Agricultural Engineers spray quality (medium), the resulting EECs did **not** result in any exceedances of the LOC for aquatic organisms when the addition of a 1 m spray buffer zone is included. These results, presented in Table 24 of PRD2022-01, indicate that the potential risks from tiafenacil to aquatic organisms exposed to tiafenacil from spray drift are mitigated with a 1 m spray buffer zone.

Comments on the use directions (minimum spray volume)

ISK Biosciences Corp. (the registrant) submitted a comment proposing to revise the minimum spray volume from 140 to 100 liters of final spray solution per hectare on the labels for Tiafenacil 70WG Herbicide (Sub. No. 2018-1276) and Insight 339SC Herbicide (Sub. No. 2018-1301), since they determined that the minimum spray volume of 140 liters of final spray solution per hectare defined in the initial labels submitted is not in line with the typical practices of application of many Canadian growers. The registrant's rationale states that the efficacy trial data submitted in support of the proposed registrations included many trials with application spray volumes of 100 liters or less; and that the change provides Canadian farmers with greater operational flexibility enabling the use of less fuel to apply product to a wider area when it is advantageous to do so.

Health Canada response

The proposed revision of the minimum spray volume from 140 L/ha to 100 L/ha is supported, based on the assessments below.

Value and efficacy: Since the proposed change will result in the spray volume decreasing, and both tiafenacil end-use products will not be applied directly to any host crops, efficacy will be the greatest concern for this proposed amendment.

The PMRA reviewed the relevant tiafenacil trial data to determine what application volumes were evaluated in the trials for which data were provided for review. Tables 1 and 2 summarize the relevant trial data that were provided for the eight weed species the PMRA was able to support for labelling at 25 to 50 g ai/ha.

Table 1 Efficacy observations for trials that evaluated the early-season control of supported weeds using tiafenacil applied at 100 L/ha (or less)

Weed	Trials and application volume	Efficacy observations for 100 L/ha (or less)
Kochia	3 trials @ 187 L/ha	-
	2 trials @ 140 L/ha	-
	1 trial @ 100 L/ha	greater than 94% control up to 24 DAT
	2 trials – not reported	-
Russian thistle	2 trials @ 187 L/ha	-
	1 trial – not reported	-
Velvetleaf	2 trials @ 187 L/ha	-
	1 trial @ 93.5 L/ha	100% control up to 7 DAT

DAT = Day after treatment

Table 2 Efficacy observations for trials that evaluated the early-season suppression of supported weeds using tiafenacil applied at 100 L/ha (or less)

Weed	Trials and application volume	Efficacy observations for 100 L/ha (or less)
Lamb's-quarters	8 trials @ 187 L/ha	-
	1 trial @ 157 L/ha	-
	2 trials @ 140 L/ha	-
	1 trial @ 100 L/ha	Suppression level of control up to 27 DAT
	1 trial @ 93.5 L/ha	100% control up to 7 DAT
	1 trial not reported	-
Prickly lettuce	2 trials @ 187 L/ha	-
	1 trial @ 140 L/ha	-
	2 trials – not reported	-
Redroot pigweed	3 trials @ 187 L/ha	-
	1 trial @ 157 L/ha	-
	2 trials – not reported	-
Tall Waterhemp	1 trial @ 187 L/ha	-
	1 trial @ 159 L/ha	-
Wild buckwheat	2 trials @ 100 L/ha	Suppression level of control up to 28 DAT

DAT = Day after treatment

The current supported spray volume wording on both tiafenacil end-use product labels reads as (italicized text): "*The minimum spray volume for applications of Tiafenacil 70WG/339SC Herbicide is 140 liters of final spray solution per hectare. When targeting dense weed populations and/or mature weeds, use higher spray volumes.*"

Although the trial data currently in-house are limited for application volumes of 100 L/ha (or less), the PMRA can support the proposed reduction in the minimum application volume given the following:

1) Efficacy observations for trials that evaluated application volumes of 100 L/ha (or less) corresponded with the overall efficacy that was observed over all trials / application volumes for kochia, velvetleaf, lamb's-quarters and wild buckwheat.
2) These four weed species are agronomically important and generally considered to be difficult to control.
3) Other Group 14 Herbicides are labelled for use at an application volume of 100 L/ha.

Dietary exposure: The change in spray volume is not expected to impact the magnitude of tiafenacil residues in/on treated crop commodities given that:

- The tiafenacil residues from the field trials were generated using a range of spray volumes: 196–383 L/ha for grapes, 187–337 L/ha for corn, 187–290 L/ha for soybean and 178–337 L/ha for wheat.
- The timing of applications during the field trials was representative of the proposed labels. Applications were made to the soil prior to planting or prior to crop emergence for corn, soybean and wheat, and were directed under the foliage for grapes. As such, there should be no direct contact of the tiafenacil residues with the crops.

The revision of the minimum spray volume from 140 L/ha to 100 L/ha can be supported from a dietary exposure perspective.

Occupational exposure: Taking into account the requested change in spray volume, which results in an increase in the amount of active ingredient handled per day, the mixer/loader/applicator risk assessment for the two end-use products were updated. Calculated margin of exposures (MOEs) are greater than the target MOE of 100 for all chemical handler scenarios for agricultural crops and non-cropland areas, and therefore, no health risks of concern were identified with the proposed reduction in spray volume (see Tables 3 and 4 below).

Table 3 Updated Mixer/Loader/Applicator Risk Assessment for Tiafenacil 70WG Herbicide

Exposure scenario	Unit exposure (µg/kg a.i. handled)[1]		ATPD (ha/day)[2]	Rate (kg a.i./ha)	Daily exposure (mg/kg bw/day)[3]		MOE[4]	
	Dermal	Inhalation			Dermal	Inhalation	Dermal	Inhalation
PPE for all scenarios: Single layer and chemical-resistant gloves								
Open Mix/Load Dry Flowable + Open Cab Groundboom	109.5	23.5	107	0.050	7.38×10^{-3}	1.58×10^{-3}	1.35×10^{5}	1074
			360		2.48×10^{-2}	5.33×10^{-3}	4.03×10^{4}	319
Open Mix/Load Dry	1027.5	67.0	1.5	0.050	9.71×10^{-4}	6.33×10^{-5}	1.03×10^{6}	2.69×10^{4}

Exposure scenario	Unit exposure (µg/kg a.i. handled)[1]		ATPD (ha/day)[2]	Rate (kg a.i./ha)	Daily exposure (mg/kg bw/day)[3]		MOE[4]	
	Dermal	Inhalation			Dermal	Inhalation	Dermal	Inhalation
PPE for all scenarios: Single layer and chemical-resistant gloves								
Flowable + Low Pressure Handwand								
Open Mix/Load Dry Flowable + Backpack	5530.0	83.9	1.5	0.050	5.23×10^{-3}	7.93×10^{-5}	1.91×10^{5}	2.14×10^{4}
Open Mix/Load Dry Flowable + High Pressure Handwand	5669.6	172.8	38	0.050	1.36×10^{-1}	4.14×10^{-3}	7.37×10^{3}	411
Open Mix/Load Dry Flowable + Right-of-Way Sprayer	956.7	26.8	38	0.050	2.29×10^{-2}	6.42×10^{-4}	4.37×10^{4}	2650

ATPD = Area treated per day; MOE = Margin of exposure; PPE = Personal protective equipment

[1] Unit exposure estimates based on AHETF data for open mixing/loading a dry flowable and groundboom application, and PHED for all other application equipment.

[2] Default Area Treated per Day table (2017-09-20), ATPDs for handheld and ROW equipment were calculated using the formula ATPD (ha/day) = Liters applied per day (3800 L/day for mechanically-pressurized handwand and ROW sprayer, and 150 L/day for manually-pressurized handwand and backpack sprayer) ÷ spray volume (100 L/ha)

[3] Daily exposure = (Unit exposure × ATPD × Rate) / (80 kg bw × 1000 µg/mg)

[4] Based on dermal NOAEL = 1000 mg/kg bw/day; inhalation NOAEL = 1.7 mg/kg bw/day; and target MOE = 100 for all exposure scenarios.

Table 4 Updated Mixer/Loader/Applicator Risk Assessment for Insight 339SC Herbicide

Exposure scenario	Unit exposure (µg/kg a.i. handled)[1]		ATPD (ha/day)[2]	Rate (kg a.i./ha)	Daily exposure (mg/kg bw/day)[3]		MOE[4]	
	Dermal	Inhalation			Dermal	Inhalation	Dermal	Inhalation
PPE for all scenarios: Single layer and chemical-resistant gloves								
Open Mix/Load Liquid + Open Cab Groundboom	83.9	2.31	107	0.050	5.63×10^{-3}	1.55×10^{-4}	1.78×10^{5}	1.10×10^{4}
			360		1.89×10^{-2}	5.28×10^{-4}	5.22×10^{4}	3.26×10^{3}
Open Mix/Load Liquid + Low Pressure Handwand	943.4	45.2	1.5	0.050	8.88×10^{-4}	4.25×10^{-5}	1.13×10^{6}	4.00×10^{4}
Open Mix/Load Liquid + Backpack	5445.9	62.1	1.5	0.050	5.13×10^{-3}	5.85×10^{-5}	1.95×10^{5}	2.91×10^{4}

Exposure scenario	Unit exposure (µg/kg a.i. handled)[1]		ATPD (ha/day)[2]	Rate (kg a.i./ha)	Daily exposure (mg/kg bw/day)[3]		MOE[4]	
	Dermal	Inhalation			Dermal	Inhalation	Dermal	Inhalation
PPE for all scenarios: Single layer and chemical-resistant gloves								
Open Mix/Load Liquid + High Pressure Handwand	5585.5	151	38	0.050	1.33×10^{-1}	3.60×10^{-3}	7.51×10^{3}	472
Open Mix/Load Liquid + Right-of-Way Sprayer	931.0	5.63	38	0.050	2.22×10^{-2}	1.34×10^{-4}	4.50×10^{4}	1.27×10^{4}

ATPD = Area treated per day; MOE = Margin of exposure; PPE = Personal protective equipment

[1] Unit exposure estimates based on AHETF data for open mixing/loading a liquid and groundboom application, and PHED for all other application equipment.

[2] Default Area Treated per Day table (2017-09-20), ATPDs for handheld and ROW equipment were calculated using the formula ATPD (ha/day) = Liters applied per day (3800 L/day for mechanically-pressurized handwand and ROW sprayer, and 150 L/day for manually-pressurized handwand and backpack sprayer) ÷ spray volume (100 L/ha)

[3] Daily exposure = (Unit exposure × ATPD × Rate) / (80 kg bw × 1000 µg/mg)

[4] Based on dermal NOAEL = 1000 mg/kg bw/day; inhalation NOAEL = 1.7 mg/kg bw/day; and target MOE = 100 for all exposure scenarios.

The revision of the minimum spray volume from 140 L/ha to 100 L/ha can be supported from an occupational exposure perspective.

Other information

The relevant confidential test data on which the decision is based (as referenced in PRD2022-01, *Tiafenacil, Tiafenacil 70WG Herbicide, Tiafenacil 339SC Herbicide*) are available for public inspection, upon application, in the PMRA's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

Any person may file a notice of objection[2] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of Canada.ca (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[2] As per subsection 35(1) of the *Pest Control Products Act.*

List of abbreviations

µg	microgram
ADI	acceptable daily intake
ASAE	American Society of Agricultural Engineers
ATPD	area treated per day
CFIA	Canadian Food Inspection Agency
CRA	cumulative risk assessment
DAT	day after treatment
EEC	estimated environmental concentrations
EFSA	European Food Safety Authority
ha	hectare
HFC	hydrofluorocarbons
HCFC	hydrochlorofluorocarbons
HFO	hydrofluoroolefines
kg	kilogram
L	litre
MBS	market basket survey
mg	milligram
MOE	margin of exposure
MRL	maximum residue limit
NA	not applicable
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
PDP	Pesticide Data Program
PHED	Pesticide Handler Exposure Database
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PPO	protoporphyrinogen IX oxidase
PRD	Proposed Registration Decision
RD	Registration Decision
TFA	trifluoroacetic acid
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency

References

European Food Safety Authority. (2014). Reasoned opinion on the setting of MRLs for saflufenacil in various crops, considering the risk related to the metabolite trifluoroacetic acid (TFA). EFSA Journal, 12(2), 3585. https://www.efsa.europa.eu/en/efsajournal/pub/3585

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