Proposed Re-evaluation Decision PRVD2014-05

Flumetsulam

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide flumetsulam, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing flumetsulam for sale and use in Canada.

An evaluation of available scientific information found that products containing flumetsulam do not present unacceptable risks to human health or the environment when used according to the proposed label directions. As a condition of the continued registration of flumetsulam uses, new risk reduction measures are proposed for the end-use product registered in Canada. No additional data are being requested at this time.

This proposal affects the products containing flumetsulam registered in Canada. Once the final re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for flumetsulam and presents the reasons for the proposed re-evaluation decision. It also proposes new risk reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of flumetsulam.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach which is in line with the requirements of the *Pest Control Products Act*.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

What Is Flumetsulam?

Flumetsulam is a selective herbicide which belongs to the triazolopyrimidine family and is classified as a Group 2 herbicide. Flumetsulam is an inhibitor of the plant enzyme acetolactate synthase. In Canada, it is currently registered for control of broadleaved weeds in hybrid field corn and soybeans in Eastern Canada only. Flumetsulam is applied by ground equipment only.

Health Considerations

Can Approved Uses of Flumetsulam Affect Human Health?

Flumetsulam is unlikely to affect your health when used according to the proposed label directions.

People could be exposed to flumetsulam by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Flumetsulam is unlikely to affect human health provided that risk-reduction measures proposed by the PMRA to further protect workers who handle the product are implemented.

Environmental Considerations

What Happens When Flumetsulam Is Introduced Into the Environment?

Flumetsulam poses a potential risk to terrestrial and aquatic plants, therefore additional risk reduction measures need to be observed.

When flumetsulam is released into the environment, some of it can be found in soil and surface water. In the terrestrial environment, flumetsulam is expected to be non-persistent to moderately persistent; no major transformation products are produced in soil. Flumetsulam is shown to bind weakly to soils and may have the potential to leach into groundwater, particularly in well drained, low organic matter soil.

In aquatic environments, flumetsulam is expected to be persistent; no major transformation products are produced in water under aerobic conditions. Under anaerobic conditions, flumetsulam is shown to transform to a single major product, reduced flumetsulam-hydrate which is expected to be persistent. In aquatic environments, flumetsulam and reduced flumetsulam-hydrate are expected to remain in the water phase with very little partitioning to sediments. Flumetsulam residues are not expected in the air because of its low volatility and it has a low potential for bioaccumulation in biota.

Flumetsulam may pose a risk to terrestrial and aquatic organisms. In order to minimize the potential exposure of aquatic organisms to flumetsulam, an unsprayed area (spray buffer zone) is needed between the sprayer and downwind sensitive habitats. The width of these spray buffer zones will be specified on the product label.

Proposed Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of flumetsulam, the PMRA is proposing further risk-reduction measures for product labels:

Human Health

- Additional precaution statements to protect workers during handling of the product and bystanders from spray drift are required;
- A restricted-entry interval (REI) of 12 hours to protect workers entering treated sites is required; and
- A pre-harvest interval (PHI) of 90 days for soybean is required.

Environment

- Precautionary statements and spray buffer zones for non-target aquatic habitats are required; and
- To reduce the potential for run off of flumetsulam to adjacent aquatic habitats, precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted are required.

Residues of flumetsulam have a high potential to leach, therefore, a label statement is required advising that flumetsulam has the potential to reach groundwater, particularly in areas where soils are permeable and/or the depth to the water table is shallow.

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

Next Steps

Before making a final re-evaluation decision on flumetsulam, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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

Science Evaluation

1.0 Introduction

Flumetsulam is a selective herbicide that acts by inhibiting plant enzyme acetolactate synthase. This active ingredient belongs to the triazolopyrimidine family and is classified as a Group 2 herbicide.

Following the re-evaluation announcement for flumetsulam, the registrant of the technical grade active ingredient in Canada indicated continued support for all uses included on the label of the commercial class end-use products currently registered in Canada.

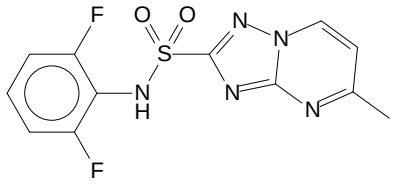
Currently registered products containing flumetsulam are listed in Appendix I. All current uses are being supported by the registrant and were, therefore, considered in the re-evaluation of flumetsulam.

The purpose of this re-evaluation is to review existing information on the active ingredient, flumetsulam, and the currently registered flumetsulam technical and commercial class end-use products, to ensure that previous risk assessments meet current standards.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Flumetsulam
Function	Herbicide
Chemical family	Triazolopyrimidine
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	2′,6′-difluoro-5-methyl[1,2,4]triazolo[1,5-*a*]pyrimidine-2-sulfonanilide
2 Chemical Abstracts Service (CAS)	*N*-(2,6-difluorophenyl)-5-methyl[1,2,4]triazolo[1,5-*a*]pyrimidine-2-sulfonamide
CAS Registry Number	98967-40-9
Molecular formula	$C_{12}H_9F_2N_5O_2S$

Structural formula	
Molecular weight	325.3
Registration Number	24449
Purity of the technical grade active ingredient	98.0% nominal

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including Toxic Substances Management Policy (TSMP) Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	3.7×10^{-7} mPa
Ultraviolet (UV) / visible spectrum	Acid Media (0.08 N HCl) λ = 213.3 nm $\varepsilon = 3.80 \times 10^{4}$ M^{-1} cm^{-1} λ = 268.1 nm $\varepsilon = 6.36 \times 10^{3}$ M^{-1} cm^{-1} Neutral media (Milli-Q water) λ = 210.6 nm $\varepsilon = 3.88 \times 10^{4}$ M^{-1} cm^{-1} λ = 275.9 nm $\varepsilon = 6.52 \times 10^{3}$ M^{-1} cm^{-1} Basic Media (0.08 N NaOH) λ = 277.2 nm $\varepsilon = 7.02 \times 10^{3}$ M^{-1} cm^{-1} No observed absorbance above 320 nm.
Solubility in water at 25°C	pH Solubility (g/L) 2.5 0.049 7.0 5.65
n-Octanol/water partition coefficient at 25°C	Log K_{ow} = −0.68; K_{ow} = 0.21
Dissociation constant	pK_a = 4.6

2.3 Description of Registered Flumetsulam Uses

Flumetsulam is currently registered for use as a selective herbicide for the control of broadleaved weeds in hybrid field corn and soybeans in Eastern Canada only. Flumetsulam is registered for one application per growing season with an application rate ranging from 50 to 70 g a.i./ha. It is applied by ground equipment only.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Occupational exposure to flumetsulam may occur while working as a mixer/loader/applicator or by entering treated sites.

When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

3.1 Toxicology Summary

Flumetsulam is rapidly absorbed and excreted with little degradation and no bioaccumulation after oral administration in rats.

Flumetsulam has low oral and dermal toxicity and slight toxicity via the inhalation route. Flumetsulam is non-irritating to the skin and minimally irritating to the eyes. Flumetsulam is not a skin sensitizer. The following warning statements are required on the label of the technical product: “CAUTION-POISION” and “Harmful if inhaled”.

Following repeated short- and long-term oral dosing in several species, the most common finding was renal toxicity based on kidney lesions and associated effects in clinical chemistry and urinalysis. Chronic toxicity in mice and rats resulted in renal effects at the highest dose tested; however, flumetsulam was not determined to be oncogenic. Repeated short-term (21-day) dermal application of flumetsulam to rabbits resulted in no evidence of treatment-related systemic toxicity at doses up to 1000 mg/kg bw/day.

There was no evidence of mutagenicity or genotoxicity. There were no reproductive or developmental concerns identified for flumetsulam.

Appendix II provides an overview of flumetsulam toxicological endpoints used by the PMRA in human health risk assessments.

3.2 *Pest Control Products Act* Hazard Consideration

The *Pest Control Products Act* factor was not established as part of this assessment and is therefore not incorporated into the quantitative risk assessment.

The database contains the full complement of required studies, including developmental toxicity studies in rats and rabbits, and a multi-generational toxicity study in rats.

Increased susceptibility of fetuses following in utero exposure, relative to the dams, was not observed in rat reproduction or rand and rabbit developmental toxicity studies. No malformations occurred at any dose in the examined studies.

Based on the information above, a qualitative assessment of the toxicity database suggests that the potential risks to sensitive subpopulations and the reliability of the scientific data are accounted for by the current assessment.

3.3 Occupational Exposure

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to flumetsulam through mixing, loading or applying the herbicide or when entering a treated site to conduct activities such as scouting and/or handling treated crops.

3.3.1 Mixer/Loader/Applicator Exposure and Risk

Based on the currently registered flumetsulam use pattern, exposure to flumetsulam is expected to be mainly via dermal and inhalation routes for handlers. Exposure duration is expected to be short- to intermediate-term duration. The following exposure scenarios were identified:

- Mixing and loading of solutions and application using an open-cab groundboom sprayer;
- Mixing and loading of wettable granules and application using an open-cab groundboom sprayer; and
- Mixing and loading of wettable granules packaged in water-soluble packaging and application using an open-cab groundboom sprayer.

A quantitative assessment for mixing/loading of liquid formulations and groundboom application was previously conducted by the PMRA. The combined dermal plus inhalation exposure for workers wearing single layer clothing and gloves during mixing/loading, and single layer clothing (no gloves) during application was not of concern (MOE = 160,000; target MOE = 100). The exposure assessment for the solution formulation scenario was expected to be sufficient to encompass the wettable granule formulation.

Although certain default values have been revised since the previous PMRA assessment, the previous assessment provides sufficient protection to account for these differences. It is concluded that there are no occupational handler concerns with respect to flumetsulam products under current conditions of use.

3.3.2 Postapplication Exposure and Risk

Based on the currently registered use-pattern, flumetsulam products are applied preplant, pre-emergence, or early post-emergence. Due to the early application timing, postapplication exposure to workers re-entering treated fields for the purpose of scouting, irrigation and hand weeding is expected to be minimal.

A flumetsulam postapplication exposure assessment was previously conducted by the PMRA for workers entering treated corn fields. Postapplication exposure was not of concern on the day of application (MOE = 9000, target MOE = 100).

Although certain default values have changed since the original assessment, the estimated MOE still provides sufficient protection to account for these differences. The assessment is considered adequate and it is concluded that there are no concerns with respect to postapplication exposure for workers.

The standard 12-hour restricted-entry interval (REI) is proposed based on current PMRA practices. The proposed label statements are listed in Appendix V.

3.4 Non-occupational Exposure

3.4.1 Residential Exposure and Risk

There are no residential uses of flumetsulam in Canada. Bystander exposure is expected to be minimal and limited to exposure from drift. Certain labels contain statements pertaining to drift. A standardized statement should be added to all the labels to specify that application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.4.2 Dietary Exposure and Risk

Flumetsulam is registered in Canada for use on hybrid field corn and soybean. Canadian MRLs are established at 0.05 ppm for soybean (dry) and field corn.

The flumetsulam acceptable daily intake (ADI) is 1.0 mg/kg bw/day based on a no observed effect level (NOEL) of 100 mg/kg bw/day from a one-year oral study in the dog and a composite assessment factor of 100. No acute dietary exposure assessment or cancer dietary exposure assessment is required for flumetsulam.

A flumetsulam chronic dietary exposure assessment (DEA) was previously conducted by the PMRA using the Dietary Exposure Evaluation Model (DEEM™, version 7.075) which incorporated consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals. The assessment included soybean, corn and animal commodities.

Chronic dietary exposure (from food only) was less than 0.5% of the ADI for all population sub-groups. The highest exposed population subgroup was non-nursing infants. The exposure estimate from drinking water, based on newly available data, is less than the estimate used in the previous DEA. Therefore an updated dietary risk assessment is not required. In conclusion, exposure from food and drinking water was also below the level of concern.

The large margin between the reference dose and the exposure estimate calculated in the assessment is expected to be protective of flumetsulam residues in domestic and imported foods. As there is currently no preharvest interval (PHI) for soybean, a PHI of 90 days is proposed. The 90-day PHI is consistent with that of field corn and is supported by the available Canadian soybean residue data.

3.4.3 Aggregate Exposure and Risk

Aggregate risk combines the different routes of exposure to flumetsulam (for example, from food, water and residential exposures). Residential exposure to flumetsulam is expected to be negligible. Therefore, aggregate exposure is limited to exposure from food and drinking water. Based on the flumetsulam dietary exposure assessment, aggregate dietary exposure from food and drinking water is not of concern.

3.5 Cumulative Exposure and Risk

A common mechanism of action has not been found for flumetsulam and other pesticide products, nor is this active ingredient considered to produce a metabolite common to other pesticide active ingredients. Therefore, a cumulative risk assessment is not required.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Flumetsulam enters the terrestrial environment when it is used as a herbicide on corn and soybean. Based on its physical properties, flumetsulam is highly soluble in water and has a low potential to volatilize from moist soil or water surfaces (Henry's law constant = 7.571×10^{-9} atm m^3/mol). Hydrolysis and photolysis (in soil and water) are not considered to be important routes of transformation for flumetsulam in the environment.

In the terrestrial environment, flumetsulam is expected to be non-persistent to moderately persistent under aerobic conditions (DT_{50} = 12.4 – 150 days). Aerobic biotransformation is shown to be more rapid at higher pH and lower organic carbon. No transformation products above 10% of applied radioactivity were identified in aerobic soil. Adsorption data indicate that flumetsulam is highly mobile in soils (Koc = 4 – 15); the results of a laboratory leaching study

show that flumetsulam residues are capable of leaching through soil. The leaching assessment using Groundwater Ubiquity Score (GUS) indicates that flumetsulam will leach in soil and satisfies most of the criteria of Cohen et al. 1984 (PMRA#1918520). In Canadian terrestrial field dissipation studies, flumetsulam residues were not detected beyond 15 cm soil depth. However, in American terrestrial field dissipation studies done in relevant ecoregions, flumetsulam residues are shown to move up to 120 cm in small amounts in well drained, low organic matter soil when rain falls shortly after application. Currently there is no available groundwater monitoring data for flumetsulam in Canada, however, in the U.S.A. flumetsulam residues have been detected in groundwater. Flumetsulam residues have been detected in surface water in Canada (Appendix IV).

In aquatic environments, flumetsulam is expected to be persistent under aerobic conditions and to remain in the water phase with very little partitioning to sediments. No major transformation products were identified in a laboratory aerobic aquatic biotransformation study that was conducted for a short duration (56 days). Under anaerobic conditions, flumetsulam transformed to a single major product, reduced flulmetsulam-hydrate, which preferentially partitions to the water phase. Both flumetsulam and reduced flumetsulam-hydrate are expected to be persistent under anaerobic conditions.

The log octanol/water partitioning coefficient for flumetsulam (K_{ow} = 0.21) suggests that it will not bioaccumulate in the food chain. Environmental fate data for flumetsulam and its transformation products, in the terrestrial and aquatic environment, are summarized in Table 1 and 2 of Appendix III, respectively.

4.2 Environmental Exposure and Risk Assessment

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Expected environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the RQ is then compared to the level of concern (LOC). If the screening level RQ is below the level of

concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the LOC, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A risk assessment of flumetsulam to terrestrial organisms was based upon an evaluation of toxicity data for the following:

- one earthworm species (acute exposure)
- one bee species (acute exposure)
- two bird species (acute, reproduction exposure)
- one mammal species (acute, reproduction exposure)
- twelve plant species (seedling emergence and vegetative vigor)

A summary of terrestrial toxicity data for flumetsulam is presented in Appendix III, Table 3. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with flumetsulam.

Terrestrial Invertebrates

The screening level risk assessment for terrestrial invertebrates is summarized in Appendix III, Table 4. Earthworms are at negligible risk of ecological effects from exposure to flumetsulam as the RQs are several orders of magnitude lower than the level of concern (RQ = < 0.00003 for acute effects). For acute contact toxicity to bees the LD_{50} is > 100 µg a.i./bee, equivalent to 112 kg a.i./ha. This value is approximately 1600 times the maximum single application rate for flumetsulam (70 g a.i./ha), therefore, there is a negligible risk of acute adverse effects to honey bees due to exposure to flumetsulam.

Terrestrial Plants

Non-target plants could be exposed to flumetsulam by overspray and spray drift. The risk to non-target plants was assessed based on an EC_{25} of 0.1 g a.i./ha based on reduced vegetative vigour for rape (reduced shoot length). At the maximum single seasonal rate of 70 g a.i/ha, the RQ (EEC/EC_{25} = 700) greatly exceeds the PMRA's level of concern.

An EEC for flumetsulam resulting from spray drift was estimated based on the maximum percentage rate (% spray drift) that will drift from the application site during spraying onto areas 1 m downwind from the edge of the spray swath. The percent drift expected from the use of groundboom sprayer equipment using a coarse ASAE (American Society of Agricultural Engineers) droplet size, is 3%. At the maximum seasonal crop application rate of 70 g a.i./ha, the RQs for spray drift ($EEC/EC_{25} = 21$) exceeds the LOC. This screening assessment triggers the calculation of buffer zones in order to protect non-target plants from spray drift.

Terrestrial vertebrates

Wild birds and mammals may be exposed to residues of flumetsulam as a result of sprayed vegetation and/or contaminated prey. Standard exposure scenarios on vegetation and other food sources based on correlations in Hoerger and Kenaga (1972) (PMRA#1918526) and Kenaga (1973) (PMRA#1918527) and modified according to Fletcher et al. (1994) (PMRA#1918522) were used to determine the concentration of pesticide in the diet of small wild birds and mammals. Exposure is dependent on the body weight of the organism and the amount and type of food consumed. In the screening level assessment a set of generic body weights was used for birds and mammals (20, 100 and 1000 g, and 15, 35, 1000 g, respectively) to represent a range of small wild bird and small mammal species. It is noted that diets of animals can be highly variable from season to season as well as day to day. Furthermore, animals are often opportunists and if they encounter an abundant and/or desirable food source, they may consume large quantities of that food. For these reasons, the screening level assessment uses relevant food categories or feeding guilds for each size group consisting of 100% of a particular dietary item. At the screening level, only one feeding guild for each category of bird and mammal weights is selected. The selected feeding guilds are relevant to each specific size of bird or mammal and based on the most conservative residue values (maximum residues determined in the Hoeger and Kenega nomogram). A diet consisting of 100% plant material is not considered realistic for small and medium sized birds (20 and 100 g) and small mammals (15 g) and, therefore, was not included in the determination of estimated daily exposures (EDEs). The most conservative exposure estimate for these categories of bird and mammal weights is associated with a diet comprised of 100% small insects.

The “leaves and leafy crops” category of the nomogram is associated with the highest exposure estimate in the assessment (300 mg a.i./kg dw diet). This category of vegetation is defined by plants with very high moisture content (comparable to lettuce and cabbage). It is very unlikely that the diets of birds and mammals would be made up of an important proportion of this food item as these do not contain sufficient nutrients to meet their daily energy requirements. Large birds are not known to purposely feed on lettuce-type crops; only some incidental ingestion has been noted when birds are feeding on insect pests on the crop; birds may also feed on young shoots of various types of crop, which would be more similar to grass-like vegetation or forage crops. For large birds (1000 g), exclusive feeding on short grass is the most conservative scenario. It is thought to be possible that small herbivorous mammals would feed on leaves and leafy crops in some situations; even though these crops may not meet all the energy requirements of a small mammal, these represent an abundant and easily accessible source of food. Flumetsulam is applied to corn and soybean, crops that are not relevant to the leafy foliage category (for example, lettuce-type crops).

Therefore, the short grass category of the nomogram, the next most conservative scenario, was chosen for medium- and large-sized mammals (35 and 1000 g).

The calculated screening level risk quotients for birds and mammals are shown in Table 5 and 6 of Appendix III, respectively. The LOC was not exceeded for birds and small wild mammals based on acute and reproductive endpoints. Flumetsulam, therefore, is expected to pose a negligible acute and reproductive risk to birds or mammals.

4.2.2 Risks to Aquatic Organisms

A risk assessment for flumetsulam to aquatic organisms was based upon an evaluation of toxicity data for the following:

- one freshwater invertebrate species (acute and chronic exposure)
- three freshwater fish species (acute and chronic exposure)
- three freshwater algae species (acute exposure)
- one freshwater vascular plant species (acute exposure)
- two estuarine/marine invertebrate species (acute exposure)
- one estuarine/marine fish species (acute exposure)
- one estuarine marine algae species (acute exposure)

A summary of aquatic toxicity data for flumetsulam is presented in Table 3 (Appendix III).

Screening Level Assessment
Aquatic organisms can be exposed to flumetsulam as a result of spray drift and run-off. To assess the potential for effects from exposure to flumetsulam, screening level EECs in the aquatic environment based on direct application to water were used as exposure estimates. The calculated EECs were those determined in 15 cm body of water for amphibians and 80 cm body of water for all other aquatic organisms.

Detailed screening level assessments of the risk from flumetsulam to aquatic organisms are summarized in Table 7, Appendix III. Toxicity endpoints for most aquatic species were several orders of magnitude higher than the screening level EECs with the exception of those for aquatic plants and algae; RQs for aquatic plants and algae exceed the LOC (RQ = 3.5).

The risk to freshwater aquatic vascular plants and algae was further characterized by taking into consideration the concentrations of flumetsulam that could be deposited in off-field aquatic habitats that are downwind and directly adjacent to the treated field through drift of spray. The spray drift data of Wolf and Caldwell (2001) was used to determine that the maximum spray deposit into an aquatic habitat located 1 metre downwind from a treated field. The maximum amount of spray that is expected to drift 1 m downwind from the application site during spraying using field sprayer equipment and a coarse spray droplet size is 3%. Using this percentage for off-site drift to non-target aquatic habitats, the offsite EEC for flumetsulam at the maximum application rate (70 g a.i./ha) is expected to be 0.26 µg/L for a water body of 80 cm depth; the LOC is not exceeded for aquatic vascular plants and algae (RQ = 0.26/ 2.5 = 0.1). Spray drift of flumetsulam, therefore, is not expected to pose a risk to these aquatic organisms.

4.2.3 Summary

Available environmental studies suggest that in the natural environment, flumetsulam is slightly to moderately persistent in soil and persistent in water. No major transformation products are produced in soil or water under aerobic conditions; under anaerobic conditions, flumetsulam is shown to transform to a single major product, reduced flumetsulam-hydrate which is expected to be persistent. In aquatic environments, flumetsulam and reduced flumetsulam-hydrate are expected to remain in the water phase with very little partitioning to sediments. Flumetsulam has the potential to leach through soil into groundwater, particularly in well drained, low organic matter soil.

At the proposed application rate and use patterns, run-off and drift of flumetsulam may pose risks to aquatic organisms and terrestrial plants. The observance of spray buffer zones can effectively mitigate the entry of spray drift into aquatic and terrestrial systems. Spray buffer zones will not mitigate runoff. To reduce the potential for runoff of flumetsulam to adjacent aquatic habitats, precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted are required. In addition, a vegetative strip between the area and the edge of a water body is recommended to reduce runoff of flumetsulam to aquatic areas

5.0 Value

Flumetsulam contributes to weed management in soybean and corn production although the acreage treated is relatively small as compared to those major soybean and corn herbicides. It is mainly used in co-formulation with other herbicides (for example, s-metolachlor or clopyralid) to broaden weed control spectrum. It is principally used in high value non-glyphosate tolerant (Identity Preserved) soybeans grown for the export market. Flumetsulam controls Eastern black nightshade which has “zero tolerance” status in food grade soybean. It provides an alternative mode of action for control of glyphosate resistant common ragweed that are becoming more prevalent in soybean and corn production. It has a wide application window (surface preplant, preplant incorporated, pre-emergence or early post-emergence) which provides growers with more flexibility in managing their farming practices, such as seeding. As a residual herbicide, flumetsulam can be tank-mixed with the non-residual glyphosate to prolong the weed-free duration which assists the crop establishment.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The TSMP is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, flumetsulam and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03 and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Flumetsulam does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix III Table 8 for comparison with Track 1 criteria.

- Flumetsulam does not form any transformation products that meet all Track 1 criteria.

The use of flumetsulam is not expected to result in the entry of TSMP Track-1 substances into the environment.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the "List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern maintained" in the *Canada Gazette*.[3] The list is used as described in the PMRA Notice of Intent NOI2005-01[4] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[5], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the flumetsulam products.

- Flumetsulam end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

7.0 Incident Reports

There are no incident reports submitted to the PMRA for products containing flumetsulam (as of 19 November 2012).

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3 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: "List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern" and in the order amending this list in the *Canada Gazette,* Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. "Part 1 Formulants of Health or Environmental Concern," "Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern."

4 NOI2005-01, List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.

5 DIR2006-02, *PMRA Formulants Policy and Implementation Guidance Document.*

8.0 Organization for Economic Co-operation and Development Status of Flumetsulam

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 34 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Flumetsulam is currently registered for use in other OECD countries, including the United States of America.

The European Commission withdrew the authorization of plant protection products containing flumetsulam in 2007. However, the European Commission decision was due to withdrawn or incomplete support for the chemical in the European review program and was not as a result of a health or environmental concern (EC, 2007).

No decision by an OECD member country to prohibit all uses of flumetsulam for health or environmental reasons has been identified.

9.0 Proposed Re-evaluation Decision

The PMRA is proposing that products containing flumetsulam for sale and use in Canada are acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment:

- Additional precaution statements to protect workers from handling and bystanders from spray drift, an REI of 12 hours to protect postapplication workers, and a PHI of 90 days for soybeans are proposed.
- Environment precautionary label statements and spray buffer zones to reduce the effects of flumetsulam in the environment are proposed.

The proposed mitigation measures are presented in Appendix V. No additional data are being requested at this time.

10.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxiques-toxics/default.asp.

List of Abbreviations

µg	microgram
1/n	exponent for the Freundlich isotherm
ADI	Acceptable Daily Intake
a.i.	active ingredient
ARfD	Acute Reference Dose
atm	atmosphere(s)
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
cPAD	Chronic Population Adjusted Dose
DACO	Data Code
DEA	Dietary Exposure Assessment
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
dw	dry weight
EC_{25}	effective concentration on 25% of the population
EDE	Estimated Daily Exposure
EDWC	Estimated Drinking Water Concentration
EEC	Expected Environmental Concentration
FC	Food Consumption
FIR	Food Ingestion Rate
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
GUS	Groundwater Ubiquity Score
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
K_d	soil-water partition coefficient
kg	kilogram(s)
K_F	Freundlich adsorption coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	Lowest Observed Adverse Effect Level
LOC	Level of Concern
LOEC	Lowest Observed Effect Concentration
LOD	Limit of Detection
LOQ	Limit of Quantitation
m^3	metre(s) cubed
mg	milligram(s)

mm Hg	millimetre mercury
MOE	Margin of Exposure
MRL	Maximum Residue Limit
nm	nanometre
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PHI	Post-Harvest Interval
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
REI	Restricted-Entry Interval
RQ	Risk Quotient
SCI-GROW	Screening Concentration in Ground Water
TC	transfer coefficient
TGAI	Technical Grade Active Ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered Flumetsulam Products as of 19 November 2013

Registration No.	Product Name	Registrant	Guarantee	Class	Formulation
24449	Flumetsulam Technical Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 98%	T	Solid
25783	Striker Manufacturing Concentrate	Dow Agrosciences Canada Inc.	Flumetsulam: 9.3% 2,4-D (present as acid): 50% Clopyralid: 25%	MC	Wettable Granules
24450	Flumetsulam 75% WDG Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 75%	C	Wettable Granules
26628	Broadstrike Dual Magnum Soybean Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 45.3 g/L S-Metolachlor and R-enantiomer 879.4 g/L	C	Solution
27004	Broadstrike RC Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 80%	C	Wettable Granules
27005	Flumetsulam 80% WDG WSP Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 80%	C	Wettable Granules
27145	Fieldstar WDG Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 18.5% Clopyralid:50%	C	Soluble Granules
27146	Fieldstar WDG WSP Herbicide	Dow Agrosciences Canada Inc.	Flumetsulam: 18.5% Clopyralid:50%	C	Soluble Granules

[1] T: Technical; MC: Manufacturing Concentrate; C: Commercial.

Appendix II Toxicological Endpoints for Flumetsulam Health Risk Assessments

Exposure Scenario	Dose[1] (mg/kg bw/day)	Study	CAF or Target MOE[2]
Acute Dietary	No endpoint established.		
Chronic Dietary	NOEL = 100	Based on renal toxicity in the 1-year feeding study in the dog	100
	ADI = 1.0 mg/kg bw/day		
Short and intermediate-term dermal	NOEL ≥ 1000	Based on lack of treatment-related effects at highest dose tested in a 21-day dermal toxicity study in rabbits	100
Short and intermediate-term inhalation	No endpoint established.		
Cancer	Flumetsulam is not oncogenic.		

[1] NOEL = No Observed Effect Level; ADI = Acceptable Daily Intake

[2] CAF = Composite Assessment Factor; Target MOE = target Margin of Exposure

Appendix III Environmental Exposure and Risk Assessment for Flumetsulam

Table 1 Summary of Fate Processes for Flumetsulam in the Terrestrial Environment

Process	$T_{1/2}$ or DT_{50}	DT_{90}	Kinetics	Comments	PMRA Reference
Abiotic transformation					
Hydrolysis: pH 5, 7 and 9, 25°C	Stable	nr	na	Not a major route of transformation	1143797
Phototransformation soil 25°C	87 – 90 d	nr	SFO	Not a major route of transformation	1143800 / 1143801
Biotic transformation					
Silt loam (Catlin)	117	2495	IORE	Moderately persistent	1143806
Sandy (Appling)	17.6	217	IORE	Slightly persistent	
Clay (Hoytville)	46.6	500	DFOP	Moderately persistent	
Loam (Webster)	94.8	928	DFOP	Moderately persistent	
Clay (Hoytville)	28.7	265	DFOP	Slightly persistent	1143808
Clay (Hoytville)	37.7	191	DFOP	Slightly persistent	1143809
Sandy loam (Tama)	35.3	173	DFOP	Slightly persistent	1143811
Sandy loam (Hanford)	45.8	152	SFO	Moderately persistent	
Silt loam (Crofton)	13.3	168	IORE	Non-persistent	
Loam (Barnes)	32.5	330	IORE	Slightly persistent	
Sandy clay loam (Milford)	70.7	1374	DFOP	Moderately persistent	
Silt loam (Hosmer)	30.9	284	IORE	Slightly persistent	
Silt loam (Putnam)	15.4	51	SFO	Slightly persistent	
Silt loam (Russel)	51.4	263	DFOP	Moderately persistent	
Silty clay loam (Sharpsburg)	36.1	207	DFOP	Slightly persistent	
Silt loam (Crofton)	24	79.8	SFO	Slightly persistent	
Silty clay loam (Sharpsburg)	32.1	145	DFOP	Slightly persistent	
Silty clay loam (Crofton)	150	630	DFOP	Moderately persistent	
Silt loam (Ida)	12.4	41.2		Non-persistent	
Sandy loam (Londo)	17.3	57.5	SFO	Slightly persistent	
Silt loam (Commerce)	22.4	74.3	SFO	Slightly persistent	
Clay (Mhoon)	45.8	152	SFO	Moderately persistent	
Clay loam (Cannisteo)	30.2	737	IORE	Slightly persistent	

Process	$T_{1/2}$ or DT_{50}		DT_{90}	Kinetics	Comments	PMRA Reference
Clay (Hoytville)	33		1253	IORE	Slightly persistent	
Clay (Perry)	51.5		1875	DFOP	Moderately persistent	
Clay (Cannisteo)	38.9		129	SFO	Slightly persistent	
Mobility						
Adsorption	Catlin silt loam	Kd = 0.34		Koc = 15	Very highly mobile	1143803
	Appling sandy loam	Kd = 0.05		Koc = 8	Very highly mobile	
	Hoytville clay	Kd = 0.18		Koc = 9	Very highly mobile	
	Webster loam	Kd = 0.19		Koc = 4	Very highly mobile	
Leaching	Soil column leaching: (Silt loam, pH 6.6, 2.52% OC, soil aged 30 days.) 39.8% of AR was found in the leachate, while 63.2% remained on the column. The first fraction (0-6 cm) contained greater than 44.6% of the applied radiocarbon (0.021 ppm). The lower fractions each contained <4% of the applied radiocarbon (0.001 ppm). Flumetsulam was the major component found by HPLC analysis of the extracts of the first column segment and leachate. Flumetsulam has a potential for leaching.					1146697
Field Studies						
Terrestrial Field Dissipation	St Thomas, ON, Canada: 16 months	40 d (SFO)	NR		At both sites, residues of flumetsulam were restricted to the upper 15 cm of the soil profile at all sampling times. Flumetsulam transformed to levels corresponding to 24 and 23% of applied mass by the end of the first season (119 and 154 days after application), and to levels corresponding to 3 and 11% of applied mass by the end of the second season (457 and 509 days after application) at the St.Thomas and the Branchton sites, respectively.	1135655
	Branchton, ON, Canada 16 months	45 d (SFO)	NR			
	Geneseo, IL, U.S.	3 months	NR		At the time of the next season's planting, 4, 9, 15, and 12% of the initial flumetsulam application was still extractable at Midland, Geneseo, Wayside and Burdette. Flumetsulam did not leach at the Geneseo or Wayside site. Trace leaching to 45 cm occurred at Midland while flumetsulam moved more apparently through the soil profile at Burdette in the 30-45 cm layer after two weeks, and an isolated detection (<2.5 µg/kg) in the 90-120 cm layer after three months.	1143813
	Wayside, MS, U.S.	3 months	NR			
	Midland MI, U.S.	1.5 months	NR			
	Burdette, MS, U.S.	1.5 months	NR			

[1] NR = Not Reported

Table 2 Summary of Fate Processes for Flumetsulam in the Aquatic Environment

Process	$T_{1/2}$ or DT_{50}	DT_{90}	Kinetics	Comments	PMRA Reference
Abiotic transformation					
Hydrolysis: pH 5, 7 and 9, 25°C	Stable	NR	NA	Not a major route of transformation	1143797
Aquatic Phototransformation	pH 5: 151 d pH 7: 727 d	NR	SFO	^{14}C-aniline label; DT_{50}s are approximate values for spring sunshine at ~ 40°N latitude and 25°c; not a major route of transformation.	1143798
	pH 5: 164 d pH 7: 330 d			^{14}C-pyrimidine label; not a major route of transformation	1143799
Aerobic biotransformation					
Pond water/sediment system	Whole system: 754 – 8824 d	NR	SFO	Persistent	1146708 / 1159712
Anaerobic biotransformation					
Water/sediment system	Whole system: 183 d	NR	SFO	Persistent	1143812

[1] NR = Not Reported; NA = Not Applicable

Table 3 Toxicity of Flumetsulam to Non-Target Species

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	PMRA Reference
Terrestrial Organisms							
Earthworm	Acute	*Eisenia foetida*	Technical (97.1%)	14-d LC_{50} 14-day NOEC	>950 mg a.i./kg soil = 950 mg a.i./kg soil	Mortality	1143843
Bee	Contact	*Apis mellifera*	Technical (99.3%)	48-h LD_{50}	> 100 µg a.i./bee	Mortality	1143842
Birds	Acute	Bobwhite quail (*Colinus virginianus*)	Technical (99.8%)	14-d LD_{50}	>2250 mg a.i./kg bw	Mortality	1143819
	Reproduction	northern bobwhite quail (*Colinus virginuanus*)	Technical (99.61%)	NOEC	18-w NOEC = 600 mg a.i./kg diet (70.9 mg a.i./kg bw/day) No effect on reproductive parameters at highest test concentration.		1143841
		mallard duck (*Anas platyrhynchos*)		NOEC	20-w NOEC = 300 mg a.i./kg diet (32.5 mg a.i./kg bw/day) Based on slight reduction in viable embryos as a percentage of eggs set.		1143823
Mammals	Acute	Rat	Technical (99.61%)	LD_{50}	> 5000 mg a.i./kg bw	Survival	1143748
	2 generation reproduction	Rat	Technical	NOEL	NOEL = 1000 mg a.i./kg/day for systemic toxicity and for reproductive and developmental toxicity, the highest dose tested.		2252169
Vascular plants	Seedling emergence	4 monocot species: corn, onion, ryegrass, oat 8 dicot species: cabbage, cucumber, lettuce, radish, rape, soybean, sugar beet, tomato.	Technical	Most sensitive species was rapeseed. NOEC = 8.5 g a.i./ha; EC_{25} = 8.9 g a.i./ha (based on reduced shoot length).			1159715
	Vegetative vigour			Most sensitive species was rapeseed. NOEC = 0.10 g a.i./ha; EC_{25} = 0.11 g a.i./ha (based on reduced shoot length).			
Freshwater Organisms							
Invertebrates	Acute	*Daphnia magna*	Technical (99.7%)	48-h LC_{50} NOEC	590 mg a.i./L 174 mg a.i./L	immobility	1143854
	Chronic	*Daphnia magna*	Technical (99%)	21-d NOEC	>200 mg a.i./L	survival and reproductive effects	1911873

Organism	Study type	Species	Test material	Endpoint	Value	Effect of concern	PMRA Reference
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Technical (99.7%)	96-h LC_{50} NOEC	>300 mg a.i./L 300 mg a.i./L	mortality	1143867
		Fathead minnow (*Pimephales promelas*)	Technical (99.7%)	96-h LC_{50} NOEC	>293 mg a.i./L 293 mg a.i./L		1143872
		Bluegill sunfish (*Lepomis macrochirus*)	Technical (99.7%)	96-h LC_{50} NOEC	>319 mg a.i./L 319 mg a.i./L		1143871
	Chronic	Fathead minnow (*Pimephales promelas*)	Technical (99.6%)	32 day early life stage NOEC LOEC	197 mg a.i./L >197 mg a.i./L	Percent hatched, percent normal larvae at hatch, survival, growth	1146724
Algae	Acute	Green algae (*Pseudokirchneriella subcapittata* –formerly known as *Selenastrum capricornutum*)	Technical (99.6%)	5-d EC_{50} NOEC	4.93 mg a.i./L 0.36 mg a.i./L	Cell density Cell density, biomass and growth rate	1143877
		Freshwater diatom *(Navicula pelliculosa)*	Technical (99.6%)	5-d EC_{50} NOEC	51.1 mg a.i./L 44.2 mg a.i./L	Cell count	19116726
		Freshwater blue-green algae *(Anabaena flos-aquae)*	Technical (99.6%)	5-d EC_{50} NOEC	0.167 mg a.i./L <0.122 mg a.i./L		1146726
Vascular Plants	Acute	Duckweed (*L. gibba*)	Technical (99.6%)	14-d EC_{50} 14-d NOEC	0.0051 mg a.i./L 0.0039 mg a.i./L	Frond count	1146725
Marine and estuarine Organisms							
>349 mg a.i/L ≥349 mg a.i/L >173 mg a.i/L	Mortality Shell deposition	Grass shrimp (*Palaemontes vulgaris*)	Technical (99.6%)	96-h EC_{50} NOEC	>349 mg a.i/L ≥349 mg a.i/L	Mortality	1143875
		Eastern oysters (*Crassostrea virginica*)	Technical (99.8%)	96-h EC_{50} NOEC	>173 mg a.i/L ≥173 mg a.i/L	Shell deposition	1143874
>379 mg a.i/L	Mortality	Atlantic silverside (*Menidia menidia*)	Technical (99.8%)	96-h EC_{50} NOEC	>379 mg a.i/L ≥379 mg a.i/L	Mortality	1143873
50 mg a.i./L 61.3 mg a.i./L	Cell count	Marine diatom *(Skeletonema costatum)*	Technical (99.6%)	120-h EC_{50} NOEC	50 mg a.i./L 61.3 mg a.i./L	Growth inhibition	1146677

[1] NA = Not Applicable; CND = Could Not Determine; NOEC = No Observed Effect Concentration; NOEL = No Observed Effect Level; LD = Lethal Dose; LC = Lethal Concentration

Table 4 Screening Level Risk Assessment for Earthworms and Bees

Organisms	Exposure	Endpoint Value	Application Rate	EEC[1]	RQ[2]
Earthworm	Acute	14-day $LC_{50} \div 2$: >425 mg a.i./kg soil	70 g a.i./ha	0.031mg a.i./kg	<0.0001
Bee	Acute contact	48-h LD_{50}: > 100 µg a.i./bee[3]	70 g a.i./ha	70 g a.i./ha	<0.01

Atkins EL; Kellum D; Atkins KW. 1981. *Reducing pesticide hazards to honey bees: mortality prediction techniques and integrated management techniques.* Univ Calif, Div Agric Sci, Leaflet 2883. 22 pp (PMRA 1573066)

[1] The Expected Environmental Concentration (EEC) in soil was calculated based on the maximum single application made to bare soil with a soil density of 1.5 g/cm^3 and even mixing through a 15 cm depth. Bee: maximum single application rate.
[2] Risk Quotient (RQ) = exposure/toxicity; Risk quotients shown in bold exceed the level of concern (RQ > 1)
[3] Toxicity in µg/bee converted to the equivalent kg a.i./ha using a conversion factor of 1.12 (Atkins et al., 1981).

Table 5 Screening Level Risk Assessment for Birds

Study type	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE[1] (mg a.i./kg bw)	RQ[1]	LOC[1] Exceeded?
Small Bird (0.02 kg)					
Acute	225	Insectivore (small insects)	3.53	0.02	No
Reproduction	32.5	Insectivore (small insects)	3.53	0.11	No
Medium Sized Bird (0.1 kg)					
Acute	225	Insectivore (small insects)	2.75	0.01	No
Reproduction	32.5	Insectivore (small insects)	2.75	0.08	No
Large Sized Bird (1 kg)					
Acute	225	Herbivore (short grass)	2.87	0.01	No
Reproduction	32.5	Herbivore (short grass)	2.87	0.09	No

[1] EDE = Estimated Daily Exposure; RQ = Risk Quotient; LOC = Level of Concern

Table 6 Screening Level Risk Assessment for Mammals

	Toxicity (mg a.i./kg bw/d)	Feeding guild (food item)	EDE[1] (mg a.i./kg bw)	RQ[1]	LOC[1] exceeded?
Small mammals (0.015 kg)					
Acute	500	Insectivore (small insects)	2.03	<0.01	No
Reproduction	1000	Insectivore (small insects)	2.03	0.002	No
Medium Sized mammals (0.035kg)					
Acute	500	Herbivore (short grass)	6.36	0.01	No
Reproduction	1000	Herbivore (short grass)	11.98	0.006	No
Large Sized mammal (1 kg)					
Acute	500	Herbivore (short grass)	3.40	0.01	No
Reproduction	1000	Herbivore (short grass)	6.40	0.003	No

EDE = Estimated Daily Exposure; RQ = Risk Quotient; LOC = Level of Concern

Table 7 Summary of the Risk of Flumetsulam to Aquatic Organisms: Screening Level

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	EEC[2] (mg a.i./L)	RQ[3]	LOC[3] exceeded
Freshwater organisms							
Invertebrate	Acute	Daphnid (*Daphnia magma*)	LC_{50} = 590	295	0.0088	<0.0001	No
	Chronic	Daphnid (*Daphnia magma*)	NOEC = 200	200	0.0088	<0.0001	No
Fish	Acute	Fathead minnow (*Pimephales promelas*)	LC_{50} >293	29.3	0.0088	<0.001	No
	Chronic		NOEC = 197	197	0.0088	<0.0001	No
Amphibian	Acute	Surrogate fish: Fathead minnow (*Pimephales promelas*)	LC_{50} > 293	29.3	0.0467	<0.01	No
	Chronic	Surrogate fish: Fathead minnow (*Pimephales promelas*)	NOEC = 197	197	0.0467	<0.001	No
Algae	Acute	Green algae (*Selenastrum capricornutum*)	EC50 = 0.0049	0.0025	0.0088	**3.5**	No
Aquatic vascular plant	Acute	Duckweed (*Lemna gibba G3*)	EC50 = 0.0051	0.0025	0.0088	**3.5**	No

Organism	Exposure	Species	Endpoint reported (mg a.i./L)	Endpoint for RA[1] (mg a.i./L)	EEC[2] (mg a.i./L)	RQ[3]	LOC[3] exceeded
Marine/Estuarine organisms							
Invertebrate	Acute	Eastern oysters (*Crassostrea virginica*)	LC_{50} >173	86.5	0.0088	<0.001	No
Fish	Acute	Atlantic silverside (*Menidia menidia*)	LC_{50} >379	37.9	0.0088	<0.001	No
Marine algae	Acute	*Skeletonema costatum*	120-h EC_{50}	61.3	0.0088	<0.001	No

[1] Endpoints used in the acute exposure Risk Assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two for aquatic invertebrates and plants, and by a factor of ten for fish and amphibians.
[2] Expected Environmental Concentration (EEC) based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms (see section 2.9.2).
[3] RQ = Risk Quotient; LOC = Level of Concern; NOEC = No Observed Effect Concentration; LC = Lethal Concentration

Table 8 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Flumetsulam: Are criteria met?
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act* [1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	No: 12.4–150 days
	Water	Half-life ≥ 182 days	Yes: >182 days
	Sediment	Half-life ≥ 365 days	Not available
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilization is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (133×10^{-15} Pa at 25°C) and Henry's Law Constant (7.57×10^{-9} atm m^3/mole).
Bioaccumulation[4]	Log $K_{OW} \geq 5$		No: 0.21
	BCF ≥ 5000		Not available
	BAF ≥ 5000		Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			**No, does not meet all TSMP Track 1 criteria.**

[1] All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).
[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4] The log L_{OW} and/or Bioconcentration Factor (BCF) and/or Bioaccumulation Factor (BAF) are preferred over *n*-Octanol/water partition coefficient (log K_{OW}).

Appendix IV Water Monitoring Data for Flumetsulam

Monitoring data were available from corn and soybean growing areas of Ontario and Quebec as well as Prince Edward Island and the Midwestern United States of America. Groundwater monitoring data were only available from the United States. A summary of the data is provided below, and in Table 8.

Although the number of monitoring studies available for flumetsulam was fairly small, the data available are considered relevant to the Canadian use pattern. The data are fairly recent (mostly collected between 2002 and 2008) and are from corn and soybean growing regions of Canada and the United States. The sampling generally occurred during summer months, which corresponds to the period of use for flumetsulam.

Based on the available data, flumetsulam seems to be routinely detected in surface water bodies located in soybean and corn growing regions of Eastern Canada and the Midwestern United States. However, the levels detected are generally quite low. The maximum detections across all areas were approximately 1.1 µg/L. However, the majority of samples had flumetsulam concentrations which were orders of magnitude below 1 µg/L. These low concentrations are likely a function of the low application rate for sulfonylurea herbicides.

Although no Canadian data were available for flumetsulam in groundwater, data from America, mainly from the NAWQA database which targets agricultural areas, indicate that flumetsulam is rarely detected in groundwater (<1% detection in approximately 2700 samples). When detected, the levels of flumetsulam were low; the maximum concentration detected in groundwater was 0.075 µg/L.

Table 1 Summary of the Monitoring Studies Available

Data Source	DETECTION FREQUENCY					CONCENTRATION (μg/L)			
	Location	Min detection or detection limit (μg/L)	# of systems tested (or absolute number of samples)	# of systems or samples with detections	% detection frequency	Mean detection	95th	Absolute max	Arithmetic mean including non-detects at ½ LOD
Flumetsulam residues in municipal drinking water sources and ground water									
PMRA 2267501	United States – treated water NAWQA (2004-2009)	0.01-0.06	159	2	1.3	0.031	0.047	0.049	0.0245
	United States – groundwater NAWQA (1999-2012)	0.011-0.1732	2717	23	0.8	0.029	0.068	0.075	0.0222
PMRA 2267516	United States – groundwater in Midwestern States (1998)	0.01	25	3	12	NA	NA	0.035	NA
PMRA 1857396	United States finished drinking water (2002)	0.006	230	3	1.3	NA	NA	0.01	NA
PMRA 1857388	United States finished drinking water (2003)	0.006-0.2	321	9	2.8	NA	NA	0.01	NA
PMRA 1852616	United States finished drinking water (2004)	0.006-0.196	233	0	0	NA	NA	NA	NA
PMRA 1852618	United States finished drinking water (2005)	0.006-0.129	230	4	1.7	NA	NA	0.01	NA
PMRA 1852619	United States finished drinking water (2006)	0.006-0.129	365	0	0	NA	NA	NA	NA
PMRA 1774484	United States finished drinking water (2007)	0.006-0.128	368	0	0	NA	NA	NA	NA
PMRA 1852614	United States finished drinking water (2008)	0.006-0.2	309	0	0	NA	NA	NA	NA

Flumetsulam residues in ambient water that may serve as a drinking water source											
PMRA 1398451, 1398452, 1398453	Corn and Soybean region of Quebec	Chibouet River	2002	0.02	42	13	31.0	0.09	0.33	0.41	0.04
			2003	0.08	41	2	4.9	0.17	0.21	0.21	0.05
			2004	0.08	37	25	67.6	0.05	0.11	0.14	0.05
		des Hurons River	2002	0.02	42	16	38.1	0.07	0.15	0.26	0.03
			2003	0.08	41	2	4.9	0.09	0.09	0.09	0.04
		Saint-Régis River	2002	0.02	40	5	12.5	0.04	0.05	0.05	0.01
			2003	0.08	39	1	2.6	0.1	0.1	0.1	0.04
		Saint-Zéphirin River	2003	0.08	39	1	2.6	0.43	0.43	0.43	0.05
PMRA 2102602	Corn and Soybean region of Quebec	Chibouet River	2005	0.007	40	16	40.0	0.014	0.02	0.023	0.008
			2006	0.007	39	13	33.3	0.01	0.017	0.021	0.006
			2007	0.007	43	2	4.7	0.012	0.014	0.014	0.004
		des Hurons River	2005	0.007	38	27	71.1	0.016	0.03	0.037	0.012
			2006	0.007	34	25	73.5	0.016	0.044	0.097	0.013
			2007	0.007	43	19	44.2	0.024	0.085	0.095	0.012
		Saint-Régis River	2005	0.007	38	1	2.6	0.007	0.007	0.007	0.004
			2006	0.007	33	3	9.1	0.031	0.054	0.057	0.006
			2007	0.007	43	3	7.0	0.016	0.019	0.019	0.004

Flumetsulam residues in ambient water that may serve as a drinking water source											
		Saint-Zéphirin River	2005	0.007	3	2	66.7	0.02	0.023	0.023	0.015
			2006	0.007	33	12	36.4	0.024	0.08	0.12	0.011
			2007	0.007	42	5	11.9	0.018	0.028	0.030	0.005
PMRA 1739256	Ontario sites (June-Sept. 2007)	Blyth		0.00131	4	3	75.0	0.0085	0.020	0.0224[2]	0.0065
		Spenser		0.00131	4	0	0	NA	NA	NA	0.0006
		Nissouri		0.00131	4	2	50.0	0.0050	0.0062	0.0068	0.0028
	Quebec sites in Yamaska River basin (June-Aug. 2007)	Noire River		0.00131	4	0	0	NA	NA	NA	0.0006
		Yamaska River		0.00131	4	1	25.0	0.0019	0.0019	0.0019	0.001
		Yamaska River at St. Hyacinth		0.00131	4	0	0	NA	NA	NA	0.0006
PMRA 2101142	Southern Ontario streams, agricultural reservoirs, urban control site		2006	0.00131	150	59	39.3	40	NA	1.1	NA
			2007	0.00131	120	16	13.3	NA	NA	0.0224	NA
			2008	0.00066	129	45	34.9	NA	NA	0.233	NA
PMRA 2267501	United States – surface water NAWQA (1999-2012)			0.011-0.1892	2825	64	2.3	0.085	0.344	1.083	0.0243
PMRA 2267500	United States – surface water in Iowa STORET (June and July 2005)			0.005	41	12	29.3	0.011	0.024	0.025	0.0049
PMRA 2267516	United States – Midwestern streams and rivers (1998)			0.01	130	82	63.1	NA	NA	0.358	NA
	United States – Midwestern reservoirs (1998)			0.01	7	4	57.1	NA	NA	NR	NA

Flumetsulam residues in water that is unlikely to be used as drinking water sources									
PMRA 1763866	PEI– surface water (Wilmot and Dunn) (2008)	0.00066	9	0	0	NA	NA	NA	0.0003
PMRA 1852616	USDA – raw water at intake to treatment plants (2004)	0.006-0.196	233	1	0.4	NA	NA	0.024	NA
PMRA 1852618	USDA– untreated water at intake to treatment plants (2005)	0.006-0.129	231	7	3.0	NA	NA	0.01	NA
PMRA 1852619	USDA – untreated water at intake to treatment plants (2006)	0.006-0.129	367	0	0	NA	NA	NA	NA
PMRA 1774484	USDA – untreated water at intake to treatment plants (2007)	0.006-0.128	362	0	0	NA	NA	NA	NA
PMRA 1852614	USDA – untreated water at intake to treatment plants (2008)	0.006-0.02	308	0	0	NA	NA	NA	NA

[1] NR = Not Reported; NA = Not Applicable, or cannot be calculated based on available data

[2] Likely the same sample as that reported in PMRA 2101142

Appendix V Proposed Label Amendments for Products Containing Flumetsulam

The label amendments presented below do not include all label requirements for individual products, such as first-aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the below label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Technical Class Product:

I) The following warning statement should appear on the **Primary** panel of the technical product labels:

- CAUTION POISON 

II) The following statements are to be added to the "**Environmental Hazards**" section of the Flumetsulam Technical products label:

- TOXIC to aquatic organisms and non-target terrestrial plants.

III) The following statements are required under the "**Precautions**" Section of the Flumetsulam Technical product label:

- Harmful if inhaled. Avoid inhaling/breathing dusts, vapours or spray mist.
- DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

Commercial Class Product:

I) The following statements must be included in a section entitled "**Precautions."**

- Do not enter or allow worker entry into treated areas during the Restricted-Entry Interval (REI) of 12 hours.
- Apply only when the potential for spray drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

II) The following statements are to be added to the "**Directions for Use**" section of products registered for use on soybean:

- The Pre-Harvest Interval (PHI) for soybean is 90 days.

III) The following statements are to be added to the "**Environmental Hazards**" section of all product labels:

- TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.
- 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 of this product when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.
- The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (*e.g.* sandy soil) and/or the depth to the water table is shallow.

IV) The following statements are required under the "**Directions for Use**" Section on all product labels:

- As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.
- DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
- Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.
- **DO NOT** apply by air.

For flumetsulam-only products:

Buffer zones:

- Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

- The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, wood lots, hedgerows, riparian areas and shrublands), and sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop	Buffer Zones Required for the Protection of: Freshwater Habitat of Depths: Less than 1 m	Buffer Zones (Metres) Required for the Protection of: Freshwater Habitat of Depths: Greater than 1 m	Buffer Zones (Metres) Required for the Protection of: Terrestrial habitat
Field sprayer	Hybrid field corn	1	1	15
Field sprayer	Soybean	1	1	20

- For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

For Broadstrike EPs (flumetsulam + S-metolachlor; Reg. Nos. 26628 and 27004):

Buffer zones:

- Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

- The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	Crop	Buffer Zones (metres) Required for the Protection of: Aquatic Habitat: Less than 1 m	Buffer Zones (metres) Required for the Protection of: Aquatic Habitat: Greater than 1 m	Buffer Zones (metres) Required for the Protection of: Terrestrial habitat
Field sprayer	Soybean	25	25	20

- For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

For Fieldstar End-use Products (flumetsulam + clopyralid; Reg. Nos. 27145 and 27146):

Buffer zones:

- Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

- The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, wood lots, hedgerows, riparian areas and shrublands), and sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop	Buffer Zones (metres) Required for the Protection of: Freshwater Habitat of Depths: Less than 1 m	Buffer Zones (metres) Required for the Protection of: Freshwater Habitat of Depths: Greater than 1 m	Buffer Zones (metres) Required for the Protection of: Terrestrial habitat
Field sprayer	Hybrid field corn	1	1	15

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

References

A. Studies considered for the Chemistry Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1423196	1991, Series 63: Physical and Chemical Characteristics of DE-498, DACO: 2.16 CBI
1418897	1991, Spectoscopic Identification of DE-498 Herbicide, AGR Sample 291668, DACO: 2.16 CBI
1916180	2010, Group A- Product Identity and Composition, Description of Materials Used to Produce the Product, Description of Production Process, Discussion of Formation of Impurities, Preliminary Analysis, Certified Limits, and Enforcement Analytical Method for Flumetsulam 98% Milled Concentrate. DACO: 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4. CBI

B. Studies considered for the Toxicological Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1143731	Xrd-498: A 2-Week Dietary Probe Study In B6C3F1 Mice (Dr-0238-5651-001)(Flumetsulam), DACO: 4.3.1
1143732	Xrd-498: A 13-Week Dietary Toxicity Study In B6C3F1 Mice Final Report (Dr-0238-5651-006)(Flumetsulam), DACO: 4.3.1
1143733	Xrd-498: 2-Week Dietary Probe Study In Fischer 344 Rats Final Report (Dr-0238-5651-003)(Flumetsulam), DACO: 4.3.1
1143735	Xrd-498: 4-Week Dietary Toxicity Study In Male Fischer 344 Rats Final Report (Dr-0238-5651-013)(Flumetsulam), DACO: 4.3.1
1143736	Xrd-498: Results Of A 13-Week Dietary Toxicity Study In Fischer 344 Rats Final Report (Dr-0238-5651-007)(Flumetsulam), DACO: 4.3.1
1143737	Xrd-498: Two Week Dietary Toxicity Probe Study In Beagle Dogs Final Report (Dr-0238-5651-016;Dr-0238-5651-016P)(Flumetsulam), DACO: 4.3.1
1143739	Xrd-498: 13-Week Dietary Toxicity Study In Beagle Dogs Final Report (Dr-0238-5651-018;-018B;-018P)(Flumetsulam), DACO: 4.3.1
1143740	Xrd-498: Probe And 21-Day Dermal Toxicity Study In New Zealand White Rabbits Final Report (Dr-0238-5651-026)(Flumetsulam), DACO: 4.3.4

1143742 Xrd-498: Two Year Chronic Toxicity/Oncogenicity Study In Fischer 344 Rats Final Report (Dr-0238-5651-014)(Flumetsulam)(Cont'D On Roll#1031), DACO: 4.4.1,4.4.2

1143748 Xrd-498: Acute Oral Toxicity Study In Fischer 344 Rats. Final Report (Dr-0238-5651-020A)(Flumetsulam), DACO: 4.2.1

1143767 (Cont'D From Roll#1030) Xrd-498: One-Year Dietary Toxicity Study In Beagle Dogs Final Report (Dr-0238-5651-024)(Flumetsulan), DACO: 4.3.1

1143768 Evaluation Of Xrd-498 In The Mouse Bone Marrow Micronucleus Test Final Report (Dr-0238-5651-009)(Flumetsulam), DACO: 4.5.4

1143769 Evaluation Of Xrd-498 In The Chinese Hamster Ovary Cell/Hypoxanthine-Guanine-Phosphoribosyl Transferase (Cho/Hgprt) Forward Mutation Assay Final Report (Dr-0238-5651-010)(Flumetsulam), DACO: 4.5.4

1143770 Evaluation Of 2,6-Difluoroaniline In The Ames Salmonella/Mammalian Microsome Bacterial Mutagenicity Assay Final Report (Dr-0275-6276-003)(Flumetsulam), DACO: 4.5.4

1143771 Xrd-498: Two-Year Dietary Oncogenicity Study In B6C3F1 Mice Final Report (Dr-0238-5651-011)(Flumetsulam)(Cont'D On Roll #1032), DACO: 4.4.2

1143773 Xrd-498: Results Of A Two-Generation Reproduction Study In Fischer 344 Rats Final Report (Dr-0238-5651-021;-021F1;-021Fa;021Fb;-021F2)(Flumetsulam), DACO: 4.5.1

1143774 Xrd-498: Dietary Teratology Study In Fischer 344 Rats Final Report (Dr-0238-5651-015)(Flumetsulam), DACO: 4.5.2

1143775 Xrd-498: Dietary Teratology Study In Fischer 344 Rats Final Report Addendum (Dr-0238-5651-015)(Flumetsulam), DACO: 4.5.2

1143776 Xrd-498: Oral Teratology Probe Study In New Zealand White Rabbits Final Report (Dr-0238-5651-017;-017A;-017B)(Flumetsulam), DACO: 4.5.2

1143777 Xrd-498: Gavage Teratology Study In New Zealand White Rabbits Final Report (Dr-0238-5651-023)(Flumetsulam), DACO: 4.5.2

1143778 Evaluation Of Xrd-498 In The Ames Salmonella/Mammalian Microsomal Mutagenicity Assay Final Report (Dr-0238-5651-002)(Flumetsulam), DACO: 4.5.4

1143780 The Evaluation Of Xrd-498 In The Rat Hepatocyte Unscheduled Dna Synthesis (Uds) Assay Final Report (Dr-0238-5651-005)(Flumetsulam), DACO: 4.5.4

1143785 Xrd-498: Two Year Dietary Oncogenicity Study In B6C3F1 Mice Final Report (Dr-0238-5651-011)(Flumetsulam), DACO: 4.4.2

1143787 The Pharmacokinetics Of Xrd-498 In Male Fischer 344 Rats And B6C3F1 Mice Final Report (Dr-0238-5651-008)(Flumetsulam), DACO: 6.4

1143807 Xrd-498: Tissue Distribution And Metabolism Of 14C-Labelled Xrd-498 In Fischer 344 Rats (Dr-0238-5651-(27)R)(Flumetsulam), DACO: 6.4

C. Studies considered for the Occupational Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

Unpublished Information

PMRA Document Number	Reference
2115788	PMRA 2011. Agricultural Reentry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients. Submission #2006-0257.

D. Studies considered for the Dietary Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1135647	De-498 Applied Preplant Incorporated To Soybeans- Residue Data For Registration & Tolerance- Canada (Res 91052)(Xrm-5019), DACO: 7.4.2
1159710	Flumetsulam Applied Preplant Incorporated/Pre-Emergence To Soybeans-Residue Data For Registration And Tolerance-Canada (Res92027), DACO: 7.4.2

E. Studies considered in the Environmental Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1143797	Aqueous Hydrolysis Of Xrd-498 (Gh-C 2092)(Flumetsulam), Daco: 8.2.1
1143798	Sunlight Photodegradation Of [14c-Aniline] Xrd-498 In A Buffered Aqueous Solution At Ph5 And 7 (Gh-C 2534;89103;211w-1;211w)(Flumetsulam), DACO: 8.2.1
1143799	Sunlight Photodegradation Of [14c-Pyrimidine] Xrd-498 In A Buffered Aqueous Solution At Ph5 And 7 (89102;210w-1;210w)(Flumetsulam), DACO: 8.2.1
1143800	Photodegradation Of [14c-Pyrimidine] Xrd-498 On Soil By Natural Sunlight (Gh-C 2452;208w;89088)(Flumetsulam), DACO: 8.2.1
1143801	Photodegradation Of [14c-Aniline] Xrd-498 On Soil By Natural Sunlight (Gh-C 2521;209w-1;209w;89089)(Flumetsulam), DACO: 8.2.1
1143803	Soil Adsorption/Desorption Of 14c-Xrd-498 (Gh-C 2159) (Flumetsulam), DACO: 8.2.4.1

1143805 A Computer Modeling Assessment Of The Mobility Of De-498 In The Three Majc Soybean Growing Regions Of The United States (Gh-C 2547)(Flumetsulam), DAC : 8.2.4.1

1143806 Aerobic Soil Degradation Of Xrd-498 (Gh-C 2160) (Flumetsulam), DACO: 8.2.3.1

1143808 Aerobic Soil Metabolism Of Aniline-Labeled De-498 In Hoytville Soil (Gh-C 2536;89002)(Flumetsulam), DACO: 8.2.3.1

1143809 Metabolism Of De-498 In Hoytville Soil At Different Temperatures (Env89002.01)(Flumetsulam), DACO: 8.2.3.1

1143811 Effect Of Soil Properties On The Degradation And Sorption Of Xrd-498 (Gh-C 2243;87062)(Flumetsulam), DACO: 8.2.3.1

1143812 Anaerobic Aquatic Metabolism Of Xrd-498 (89080)(Flumetsulam), Daco: 8.2.3.1

1143813 Terrestrial Field Dissipation Of De-498 (Env87034/An; Env88075/An)(Flumetsulam), DACO: 8.3.2.3

1146697 Aged Leaching Of [14c] De-498 In A Canadian Field Soil (Env 92004;367-W-1)(Flumetsulam), DACO: 8.2.4.1

1146708 Aerobic Aquatic Metabolism Of [14c] De-498 In Canadian Pond Water And Sediment (Env 92005-1;368w-1;17753)(Flumetsulam), DACO: 8.2.3.1

1159712 Aerobic Aquatic Metabolism Of [14c]De-498 In Canadian Pond Water And Sediment: Results Through One-Year (Env92005.02;17753;368w-2;368w)(Flumetsulam), DACO: 8.2.3.1

1135655 Terrestrial Field Dissipation Of De-498 In Eastern Canada (Env 91038)(Xrm-5019 DACO: 8.3.2.3

1135656 Evaluation Of Flumetsulam Run Off For Southern Ontario (J.Wolt; 317-337-3484)(Xrm-5019), DACO: 8.3.3.3

1143819 Xrd-498 Herbicide: An Acute Oral Toxicity Study With The Bobwhite Final Repo (103-289)(Flumetsulam), DACO: 9.6.2.1

1143820 Xrd-498 Herbicide: A Dietary Lc50 Study With The Bobwhite (103-287)(Flumetsulam), DACO: 9.6.2.1

1143821 Xrd-498 Herbicide: A Dietary Lc50 Study With The Mallard (103-288)(Flumetsulam), DACO: 9.6.2.1

1143823 Xrd-498: A One-Generation Reproduction Study With The Bobwhite (103-297)(Flumetsulam)(Cont'd On Roll# 1033), DACO: 9.6.3.1

1143841 (Cont'd Form Roll# 1032) Xrd-498 Herbicide: A One-Generation Reproduction Study With The Mallard (103-298)(Flumetsulam), DACO: 9.6.3.1

1143842 Xrd-498 Herbicide An Acute Contact Toxicity With The Honey Bee (103-290a)(Flumetsulam), DACO: 9.2.4.1

1143843 De-498 Herbicide: Toxicity To The Earthworm Final Report (39445;Es-Dr-0238-5651-18b)(Flumetsulam), DACO: 9.2.3.1

1143854 Xrd-498 Herbicide: Evaluation Of The Toxicity To Daphnia Magna Straus Final Report (Es-2001;Es-Dr-0238-5651-3)(Flumetsulam), DACO: 9.3.1

1143867 Xrd-498 Herbicide: Evaluation Of The Toxicity To Rainbow Trout Final Report (E 2002;Es-Dr-0238-5651-4)(Flumetsulam), DACO: 9.5.2.1

1143871 Xrd-498 Herbicide: Evaluation Of The Toxicity To Bluegill Final Report (Es-2000;Es-Dr-0238-5651-1)(Flumetsulam), DACO: 9.5.2.1

1143872 Xrd-498 Herbicide: Evaluation Of The Toxicity To Fathead Minnow Final Report (Es-1099;Es-Dr-0238-5651-2)(Flumetsulam), DACO: 9.5.2.1

1143873 Xrd-498 Herbicide: Acute Toxicity To Atlantic Silversides Under Flow-Through Conditions (Es-2035;89309-0300-2130)(Flumetsulam), DACO: 9.5.2.1

1143874 Xrd-498 Herbicide: Effect To New Shell Growth Of The Eastern Oyster Under Flow-Through Conditions (Es-2033;89309-0400-2130)(Flumetsulam), DACO: 9.4

1143875 Xrd-498 Herbicide: Acute Toxicity To Grass Shrimp Under Flow-Through Conditions (Es-2034;89309-0200-2130)(Flumetsulam), DACO: 9.4.1

1143877 The Toxicity Of De-498 Herbicide To Selenastrum Capricornutum (B460-11-1;Es-Dr-0238-5651-17)(Flumetsulam), DACO: 9.8.2

1146676 The Toxicity Of De-498 Herbicide To Navicula Pelliculosa (B460-13-2;Es-Dr-0235651-20)(Flumetsulam), DACO: 9.3.1

1146677 The Toxicity Of De-498 Herbicide To Skeletonema Costatum (B460-13-3;Es-Dr-0238-5651-21)(Flumetsulam), DACO: 9.3.1

1146723 De-498 Herbicide: Daphnia Magna Straus Life-Cycle (21-Day Renewal) Toxicity Test (Deco-Es-Dr-0238-5651-24)(Flumetsulam), DACO: 9.3.1

1146724 Evaluation Of The Toxicity Of De-498 Herbicide To Early Life Stages Of The Fathead Minnow Pimephlaes Promelas Rafinesque (Deco-Es-Dr-0238-5651-23)(Flumetsulam), DACO: 9.5.2.1

1146725 The Toxicity Of De-498 Herbicide To Lemna Gibba G3 (B460-13-4;Es-Dr-0238-5651-22)(Flumetsulam), DACO: 9.8.2

1146726 The Toxicity Of De-498 Herbicide To Anabaena Flos-Aquae (B460-13-1;Es-Dr-0238-5651-19)(Flumetsulam), DACO: 9.8.2

1159714 Xrm-5019 Herbicide: Effect On Short Term Respiration And Nitrogen Mineralization In A Southern Ontario Soil Final Report (93-064;Es-2698)(Flumetsulam), DACO: 9.2.7

1159715 Evaluating The Effects Of De-498 On The Germination,Emergence, And Vegetativ Vigor Of Non-Target Terrestrial Plants Final Report (40291)(Flumetsulam), DACO 9.8.4

ADDITIONAL INFORMATION CONSIDERED

Published Information

PMRA Document Number	Reference
1398451	Giroux, I. et al, 2006, Ministère du Développement durable, de l'Environnement et des Parcs, Direction du suivi de l'état de l'environnement, Direction des politiques de l'eau et Centre d'expertise en analyse environnementale du Québec., Part 1: La présen. DACO 8.6.

1398452 Giroux, I. et al, 2006, Part 2: La présence de pesticides dans l'eau au Québec, Bilan dans les cours d'eau de zones en culture de maïs et de soya en 2002, 2003 et 2004 et dans les réseaux de distribution d'eau potable. Ministère du Développement durable. DACO 8.6.

1398453 Giroux, I. et al, 2006, Part 3: La présence de pesticides dans l'eau au Québec, Bilan dans les cours d'eau de zones en culture de maïs et de soya en 2002, 2003 et 2004 et dans les réseaux de distribution d'eau potable. Ministère du Développement durable, DACO 8.6.

1918520 Cohen, S.Z., Creeger, S.M., Carsel, R.F., Enfield, C.G. 1984. Potential pesticide contamination of groundwater from agricultural uses. - ACS Symposium Series, Volume 259, Pages 297 to 325, DACO: 9.9.

1739256 Grabuski, J., Cagampan, S., Struger, J., and Bernard, R. Automated solid phase extraction of sulfonyl ureas and related herbicides in fortified water and natural water samples using LC-ESI/MS/MS. Poster presentation. Environment Canada. DACO 8.6.

1774484 United States Department of Agriculture. 2008. Pesticide Data Program Annual Summary, Calendar Year 2007. Agricultural marketing Service, Science and Technology Programs. http://www.ams.usda.gov/pdp. DACO 8.6.

1852614 United States Department of Agriculture (USDA). 2009. Pesticide Data Program Annual Summary, Calendar Year 2008. Science and Technology Programs, USDA December 2009. DACO 8.6.

1852616 United States Department of Agriculture (USDA). 2006. Pesticide Data Program Annual Summary, Calendar Year 2004. Science and Technology Programs, Agricultural Marketing Service, USDA. February 2006. DACO 8.6.

1852618 United States Department of Agriculture (USDA). 2006. Pesticide Data Program Annual Summary, Calendar Year 2005. Science and Technology Programs, Agricultural Marketing Service, USDA. November 2006. DACO 8.6.

1852619 United States Department of Agriculture (USDA). 2007. Pesticide Data Program Annual Summary, Calendar Year 2006. Science and Technology Programs, Agricultural Marketing Service, USDA. December 2007. DACO 8.6.

1857388 United States Department of Agriculture (USDA). 2005. Pesticide Data Program Annual Summary, Calendar Year 2003. Science and Technology Programs, Agricultural Marketing Service, USDA. June 2005. DACO 8.6.

1857396 United States Department of Agriculture (USDA). 2004. Pesticide Data Program Annual Summary, Calendar Year 2002. Science and Technology Programs, Agricultural Marketing Service, USDA. February 2004. DACO 8.6.

1918522 Fletcher, J.S., Nellessen, J.E., and Pfleeger, T.G. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimatir pesticide residues on plants. Environmental Toxicology and Chemistry 13:1383-1391. DACO 9.9.

1918524 Gustafson, D.I. 1989. Groundwater ubiquity score: a simple method for assessing pesticide leachability. Environmental Toxicology and Chemistry, 8: 339–357. DACO 9.9.

1918526 Hoerger F; Kenaga EE. 1972. Pesticide residues on plants: correlation of representative data as basis for estimation of their magnitude in the environment. *I* Coulston F; Korte F. (eds). Global aspects of chemistry, toxicology and technolog as applied to the environment, Vol. I. Thieme, Stuttgart, and Academic Press, Nev York. pp. 9-28. DACO 9.9.

1918527 Kenaga EE. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. In: Coulston F; Dote F. (eds). Global aspects of chemistry, toxicology and technology as applied to the environment, Vo II. Thieme, Stuttgart, and Academic Press, New York. pp. 166-181. DACO 9.9.

2101142 Struger, J., Grabuski, S. Cagampan, M. Rondeau, E. Sverko and C. Marvin. 2011. Occurrence and distribution of sulfonylurea and related herbicides in Central Canadian surface waters 2006-2008. Bulletin of Environmental Contamination and Toxicology 87:420-425. DACO 8.6.

2102602 Giroux, I. 2010. Présence de pesticides dans l'eau au Québec – Bilan dans quatre cours d'eau de zones en culture de maïs et de soya en 2005, 2006 et 2007 et dans d maïs et de soya en 2005, 2006 et 2007 et dans des réseaux de distribution d'eau potable. Ministère du Développement durable, de l'Environnement et des Parcs, Direction du suivi de l'état de l'environnement, 78 p. DACO 8.6.

2267516 Battaglin, W.A., E.T. Furlong, M.R. Burkhardt and C.J. Peter. 2000. Occurrence o sulfonylurea, sulphonamide, imidazolinone, and other herbicides in rivers, reservoi and ground water in the Midwestern United States, 1998. The Science of the Total Environment 248: 123-133. DACO 8.6.

Wolf, T.M. and B.C. Caldwell. 2001. Development of a Canadian spray drift mode for the determination of buffer zone distances. In: Expert Committee on Weeds - Comité d'experts en malherbologie (ECW-CEM). Proceedings of the 2001 Nationa Meeting, Québec City. Sainte-Anne-de-Bellevue, Québec: ECW-CEM. Eds. D. Bernier, R.A. Campbell and D. Cloutier. p. 60.

Unpublished Information

PMRA Document Number	Reference
1763866	Unpublished Pesticide Science Fund water monitoring data from the Atlantic Region (complete raw dataset from 2003-2008). Environment Canada. DACO 8.6.
2267500	United States Environmental Protection Agency. 2012. Water monitoring data for flumetsulam from the US EPA's Storage and Retrieval (STORET) Data Warehouse. Downloaded November 26, 2012. http://iaspub.epa.gov/storpubl/DW_resultcriteria_geo DACO 8.6.
2267501	United States Geological Survey National Water Quality Assessment (NAWQA) program surface water, groundwater and treated water monitoring data for flumetsulam, downloaded November 26, 2012. http://infotrek.er.usgs.gov/apex/f?p=NAWQA:HOME:0 DACO 8.6.