



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF  
CHEMICAL SAFETY AND  
POLLUTION PREVENTION

**MEMORANDUM**

**Date:** 19-SEP- 2013

**SUBJECT:** **Flumetsulam.** Preliminary Human Health Risk Assessment for Registration Review

**PC Code:** 129016

**Decision No.:** 477891

**Petition No.:** NA

**Risk Assessment Type:** Single  
Chemical/Aggregate

**TXR No.:** NA

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**Registration No.:** NA

**Regulatory Action:** Registration Review

**Case No.:** 7229

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. As part of Registration Review, the Pesticide Re-evaluation Division (PRD) of OPP has requested that HED evaluate the hazard and exposure data and conduct dietary, occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the registered uses of flumetsulam.

HED has evaluated the toxicity and exposure databases for the active ingredient, Flumetsulam, and has conducted a human health risk assessment in support of Registration Review. Based on this assessment, HED has determined that there are no potential risk estimates of concern for the currently registered uses of Flumetsulam.

A summary of the findings and an assessment of human health risk resulting from the currently registered uses of Flumetsulam are provided in this document. The HED team members contributing to this risk assessment include Mohsen Sahafeyan (risk assessment), Bridgett Bobowiec (occupational risk assessment), P. Yvonne Barnes (chemistry and dietary exposure assessment) and Yung Yang (hazard assessment). James Wolf of the Environmental Fate and Effects Division (EFED) performed the drinking water assessment for Flumetsulam.

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## 1.0 Executive Summary

As part of Registration Review, the Pesticide Re-evaluation Division (PRD) of the Office of Pesticide Programs (OPP) has requested that the Health Effects Division (HED) evaluate the hazard and exposure data and conduct dietary, occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the registered uses of Flumetsulam. This document provides a summary of the findings and an assessment of human health risk resulting from the currently registered uses of flumetsulam.

**Use Profile:** Flumetsulam (N-(2,6-difluorophenyl)-5-methyl-(1,2,4)triazolo(1,5-a)pyrimidine-2-sulfonamide) is an herbicide in the triazolopyrimidine chemical class used to control broadleaf weeds in field corn, dry bean and soybean, applied as a pre emergent and early post-emergent herbicide. HED notes that although dry bean is a registered primary crop, all labels for dry bean are inactive at present; any reference to use rate and use patterns for dry bean in this document are based on older inactive labels, field trial data, and previously reviewed occupational/residential exposure (ORE) assessment (Dow, Mark I., 2004, D306178). Flumetsulam can be applied by ground and by aerial application with restrictions. It is formulated as a water dispersible granular (WDG), a water dispersible granular packaged in water soluble packet (WSP), and as an emulsifiable concentrate (EC). The highest maximum application rate is 0.07 lb ai/A for field corn, soybeans, and dry beans.

**Hazard Assessment:** The toxicology database for flumetsulam is complete. A subchronic inhalation study was not available; however, the HED Hazard and Science Policy Council (HASPOC) determined that a subchronic inhalation toxicity study is not needed for flumetsulam at this time (TXR# 0056689).

The kidney appears to be the primary target organ of rats and dogs following exposure to high doses of flumetsulam in subchronic and chronic toxicity studies. Flumetsulam has low acute toxicity by oral, dermal, or inhalation routes of exposure. It is not a skin or eye irritant and is not a skin sensitizer. The available toxicity database shows that flumetsulam is not a neurotoxic or immunotoxic chemical and it does not induce developmental or reproductive toxicity. Flumetsulam is classified as "Group E", (evidence of non-carcinogenicity for humans); mutagenicity studies conducted with flumetsulam were negative.

An acute reference dose has not been established for either the general population or for females 13-49 years of age since there were no appropriate studies that demonstrated evidence of toxicity attributable to a single dose for these populations. For chronic dietary and other exposure scenarios, the chronic feeding study in the dog was selected because the study encompasses the appropriate exposure duration and provides a screening level hazard with a NOAEL of 100 mg/kg/day and LOAEL of 500 mg/kg/day based on renal inflammatory and atrophic changes secondary to renal calculi and hepatic effects consisting of inflammation, focal necrosis, and biliary stasis. For the dermal exposure scenario, no systemic toxicity was found in the 21-day rabbit dermal study at the limit dose (1000 mg/kg/day). Quantification of dermal risk assessment is not required for this exposure due to a lack of dermal, systemic, neuro, or developmental toxicity concerns.

The flumetsulam risk assessment team has recommended that the FQPA Safety Factor be reduced to 1X based on an adequate and complete toxicity database and exposure data. There is no evidence of qualitative or quantitative susceptibility *in utero* or during post-natal exposure in developmental and reproduction studies and there is no evidence of neurotoxicity in the submitted studies. A developmental neurotoxicity study is not required since there was no evidence of neurotoxicity or neuropathy from the available studies.

**Dietary Exposure (Food and Drinking Water):** The residue chemistry data and environmental fate data are adequate to assess human exposure. Estimated drinking water concentrations (EDWCs) from surface water and groundwater sources were generated by the Environmental Fate and Effects Division (EFED) using computer modeling methods.

Acute: An acute dietary exposure assessment was not performed as no appropriate endpoints were identified from the available flumetsulam toxicity studies for the acute dietary scenario.

Chronic: Both food and water were incorporated in the dietary exposure analysis. Tolerance-level residues and 100% crop treated assumptions for all the crops were used in the chronic dietary exposure assessment. Flumetsulam residue in water was assumed to be 14.8 ppb according to EFED's highest estimated chronic drinking water concentration. The estimated exposure for the general U.S. population and all population subgroups resulted in exposures less than 1 percentage of the chronic population adjusted dose (cPAD).

Cancer: A cancer dietary exposure assessment was not performed as flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans).

**Residential Exposure:** There are currently no registered residential uses associated with flumetsulam; therefore, a residential/non-occupational exposure assessment is not required.

**Aggregate Risk:** Aggregate risk assessments evaluate the combined risk from dietary exposure (food and water) and any non-occupational (residential) uses. There are currently no registered residential uses associated with flumetsulam; therefore, a residential/non-occupational exposure assessment is not required. As a result, the flumetsulam aggregate risk assessment includes only dietary exposure (food and water). An acute dietary exposure assessment was not performed as no appropriate endpoints were identified from the available flumetsulam toxicity studies for the acute dietary scenario. The chronic dietary exposure estimates from food and drinking water do not exceed HED's level of concern (<1% of cPAD). A cancer dietary exposure assessment was not performed as Flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans).

**Occupational Exposure/Risk:** The occupational database is complete. Occupational handler exposures to the existing uses of flumetsulam may occur via dermal and inhalation route. However, quantification of dermal risk is not required due to a lack of dermal, systemic, neuro, or developmental toxicity concerns. Therefore, only inhalation exposure was assessed for handlers.

The short- and intermediate-term inhalation risk estimates for all occupational handler scenarios do not exceed HED's level of concern, i.e., margin of exposures are greater than 100 (MOEs > 100) at baseline personal protective equipment (PPE). The flumetsulam product labels direct mixers, loaders, applicators and other handlers to wear long-sleeved shirts, long pants, waterproof gloves, and shoes plus socks. Some of the labels require the PPE to include goggles or face shields because some end use products contain a mixture of chemicals with different acute toxicity categories than flumetsulam. HED recommends that the Registration Division (RD) ensure the appropriate safety directions and a 12 hour restricted entry interval (REI) are included in the label based on the acute toxicity of flumetsulam and that products that include a formulated mixture of active ingredients should retain the 48 hour REI.

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for flumetsulam at this time primarily because of the low acute inhalation toxicity, vapor pressure and the use rates. However, since handler inhalation exposure is likely to be higher than post-application exposure and the estimates for handler inhalation exposure are below the level of concern (MOE >100), it is expected that these handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for flumetsulam.

Spray drift analysis was conducted for a hand to mouth (HtM) scenario for children ages 1<2 years of age using Tier 1 screening parameters. The aerial and ground applications of flumetsulam at the current maximum application rates resulted in MOEs not of concern for field corn, soybeans, and dry beans.

There are no label recommendations from the occupational assessment. There are no data deficiencies or additional requirements for flumetsulam at this time.

**Review of Human Research:** This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These studies (listed in Appendix C) have been determined to require a review of their ethical conduct and all of the studies utilized in this assessment have received the appropriate review.

**Data Deficiency:** The databases for toxicology, residue chemistry, occupational and residential requirements are complete. There are no outstanding data deficiencies.

## 2.0 Introduction

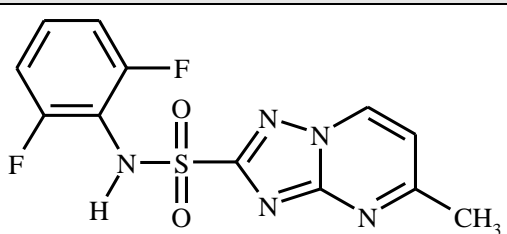
### 2.1 Tolerances

Tolerances are established for the herbicide flumetsulam under 40 CFR: §180.468 for bean, dry, seed; corn, field, forage; corn, field, grain; corn, field, stover; soybean, seed, each at 0.05 ppm.

### 2.2 International Harmonization

The Codex Alimentarius Commission has not established Maximum Residue Limits (MRLs) for residues of flumetsulam. Canadian MRLs are established for field corn and dry soybean each at 0.05 ppm; Canada does not establish MRLs on feed stuffs. No harmonization is needed. For a summary of US and International Tolerances and Maximum Residue Limits, see Appendix E.

### 2.3 Structure and Nomenclature

Table 2.3 - Flumetsulam Nomenclature	
Chemical structure	
Common Name	Flumetsulam
Company Experimental Name	DE-498 and TSN-100986
Empirical Formula	C <sub>12</sub> H <sub>9</sub> F <sub>2</sub> N <sub>5</sub> O <sub>2</sub> S
IUPAC Name	2-(2,6-difluorophenylsulphamoyl)-5-methyl(1,2,4)-Triazolo(1,5-a)pyrimidine
CAS Name	N-(2,6-difluorophenyl)-5-methyl-(1,2,4)triazolo(1,5-a)pyrimidine-2-sulfonamide
CAS Registry Number	98967-40-9

### 2.4 Physical/Chemical Characteristics

Listed in Appendix B are the physical and chemical properties as well as the relevant environmental fate parameters. Flumetsulam low vapor pressure ( $1.0 \times 10^{-15}$  mm Hg at 25.0 °C) indicates that flumetsulam is non-volatile. Flumetsulam is soluble in water and is stable under photolysis. Degradation studies indicate the aerobic soil half-life ranges from approximately two weeks to four months with the majority degrading in less than two months (mean of 69.5 days).

### 2.5 Summary of Existing Uses

Flumetsulam is a pre emergent and early post-emergent herbicide used to control broadleaf weeds in field corn, soybeans, and dry beans; HED notes that although dry bean is a registered primary crop, all labels for dry bean are inactive at present; any reference to use rate and use pattern for dry bean in this document are based on older inactive labels, field trial data, and previously reviewed ORE document (Dow, Mark I., 2004, D306178). Flumetsulam is in the triazolopyrimidine chemical class and has a mode of action similar to the sulfonylurea herbicides that are acetolactate synthase inhibitors, which regulate plant growth. Flumetsulam is formulated as water dispersible granular WDG, water dispersible granular packaged in water soluble packets WSP, and as an emulsifiable concentrate EC. Flumetsulam can also be incorporated with liquid and dry bulk fertilizer. The water soluble packets must be combined with water to create slurry first before attempting to mix with a carrier fertilizer. Some of the registered products contain a mixture of flumetsulam and additional active ingredients which are not evaluated in this registration review document.



Flumetsulam can be applied by ground and by air with restrictions. Chemigation is prohibited. Field corn and soybeans have application rates ranging from 0.035 lb ai/A to 0.07 lb ai/A. Flumetsulam application rates on dry beans range from 0.04 to 0.07 lb ai/A based on older inactive labels, field trial data, and previously reviewed ORE document (Dow, M., 2004, D306178). Rotational crop restrictions are directed on labels. Currently, there are two registered manufacturing-use products ; (EPA Reg. No. 62719-223) Flumetsulam Technical 98 % a.i., and (EPA Reg. No. 62719-300) Hornet MUP 23.1 % a.i. flumetsulam. Application rates and restrictions for all other labels are summarized in the following Table 2.5.

**Table 2.5 - Summary Use Profile for Flumetsulam**

Registration Number and Product Name	Application Equipment.	Formulation	Applic. Rate (lb a.i./A)	Max. No. Applic. Per Season	Max. Seasonal Applic. Rate (lb a.i./A)	PHI (days)	Use Directions and Limitations	RE I
<b>Field Corn</b>								
352-612 DuPont Accent Gold 15.9 % a.i.	Ground with aerial application only in following states, Colorado, Iowa, Kansas, Minnesota, Nebraska, Oklahoma, South Dakota, and Texas	Water dispersible granular packaged in a soluble packet	0.035	1	0.035	85	Do not apply to popcorn or sweet corn. Can apply to corn up to 12 inches tall and when grass and broadleaf weeds are young or pre-emergent. Adequate soil moisture is required for residual activity. Use at least 15 gallon water per acre for broadcast application and 5 gallons per acre for aerial application. Do not apply a cumulative rate of more than 0.07 lbs of flumetsulam per year.	48 hours
352-593 Accent Gold 19.1 % a.i.	Ground Broadcast or Branded							
62719-278 NAF-280 13.9 % a.i.	Ground Do not apply aerially						Preplant, surface, incorporated, preemergence, or post emergence treatment. Adequate soil moisture is required for residual activity. Must make slurry to mix with fertilizer. Apply a minimum of 200 pound of dry impregnated fertilizer	
62719-253 Hornet 23.1 % a.i.	Ground and aerially with supplemental labels New York Restrictions		0.07		0.07	85	Spray volume of 10 to 60 gallons per acre	
62719-315 Hornet WDG 18.5 % a.i.	Ground New York Restrictions		0.07		0.07		Post-emergent treatment should be applied with water	
62719-279 NAF-281 12.1 % a.i.	Ground Do not apply aerially		0.05		0.05		Do not apply aerially	

**Table 2.5 - Summary Use Profile for Flumetsulam**

Registration Number and Product Name	Application Equipment.	Formulation	Applic. Rate (lb a.i./A)	Max. No. Applic. Per Season	Max. Seasonal Applic. Rate (lb a.i./A)	PHI (days)	Use Directions and Limitations	RE I
							unless by EPA approved supplemental labeling.	
62719-570 Sure Start 1.3 % a.i		Emulsifiable concentrate	0.05	1	0.05		Contains 3 active ingredients. PPE includes gloves, eyewear, headgear, and apron. Post emergent corn can be sprayed up to 11 inches Apply a minimum of 200 pound of dry impregnated fertilizer Spray volume of 10 to 60 gallons per acre	12 hours
<b>Soybeans</b>								
62719-299 Frontrow Flumetsulam 80 WDG 80% a.i.	Ground and aerial application with supplemental labeling. Aerial application prohibited New York	Water dispersible granulars in water soluble packets	0.006	2	0.012	70	Front Row is a co-pack product. Do not mix and apply separately water – soluble packets. Use of product in Nassau and Suffolk counties in New York are prohibited. Do not graze or feed soybean forage.	12 hours
<b>Field Corn and Soybeans</b>								
62719-224 Broad Strike formerly XRM-6019 74 % a.i							Preplant, surface, incorporated, preemergence, or post emergence treatment. Application may be made to field corn up to 12 inches tall and soybeans in the first to fifth trifoliolate leaf stage. Use at least 10 gallons of spray per acre for ground application. Apply a minimum of 200 pound of dry impregnated fertilizer. Must make slurry to mix with fertilizer. Do not make post emergence applications near freezing temperatures	
62719-277 Python WDG 80 % a.i.	Ground, Aerially (no aerial application in New York)	Water dispersible granulars	0.07	1	0.07	85days for corn and soybean harvest 45 days for corn forage harvest		12 hours
<b>Dry Beans<sup>1</sup></b>								

**Table 2.5 - Summary Use Profile for Flumetsulam**

Registration Number and Product Name	Application Equipment.	Formulation	Applic. Rate (lb a.i./A)	Max. No. Applic. Per Season	Max. Seasonal Applic. Rate (lb a.i./A)	PHI (days)	Use Directions and Limitations	RE I
62719-239 Broadstrike® + Dual 20 % a.i.	Ground only	Emulsifiable concentrate	0.063	1	0.07 lb ai/acre	85 days	Products may be applied 10 - 14 days prior to planting as a soil incorporated application or as a surface application. It may be applied post-plant but prior to crop or weed emergence.	12 hours
62719-222 Broadstrike® + Treflan® 25 % a.i.			0.07					
62719-277 Broadstrike WDG 80 % a.i.		Water dispersible granule	0.067					

<sup>1</sup>Dry bean labels are inactive. Use and rates are based on older inactive labels, field trial data, and previously reviewed ORE document (Dow, Mark I., D306178).

## 2.6 Anticipated Exposure Pathways

Humans may be exposed to flumetsulam in their diet resulting from residues present in foods treated with flumetsulam. Further, given the environmental fate parameters of flumetsulam and the registered agricultural uses, the potential exists for flumetsulam to reach water resources resulting in potential residues in drinking water. There are currently no residential uses of flumetsulam, so exposure in residential and non-occupational settings is not likely. There is a potential for occupational handler and post-application exposures.

## 2.7 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations,” (<http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf>). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup’s food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture’s National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group.

Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

### **3.0 Hazard Characterization and Dose-Response Assessment**

Previously, a comprehensive risk assessment for flumetsulam was conducted in 2004 (E. Reaves, D306238, 11/22/2004) and a scoping document was issued in 2008 (S. Recore, D349638, 8/12/2008). Since then, new studies including acute and subchronic neurotoxicity and immunotoxicity studies were submitted. In addition, the Hazard and Science Policy Council (HASPOC) determined that a subchronic inhalation toxicity study is not needed for flumetsulam at this time (TXR# 0056689). Please refer to Appendix A for the hazard profile table. This assessment includes summaries of prior assessments.

#### **3.1 Summary of Toxicological Effects**

Flumetsulam has low acute toxicity by oral, dermal, or inhalation routes of exposure. It is not a skin or eye irritant and is not a skin sensitizer. The kidney appears to be the primary target organ of rats and dogs following exposure to high doses of flumetsulam in subchronic to chronic toxicity studies. Following subchronic oral exposure, rats developed bilateral tubular nephritis at concentrations equal to the limit dose; however, no renal effects were found in mice at doses five times the limit dose. In chronic dog and rat studies, renal calculi, inflammation, and atrophic changes were found in the kidney of male animals. These effects were not observed in female rats or dogs, or in treated male and female mice. There were no evidences of neurotoxicity, immunotoxicity, developmental, or reproductive toxicity in the submitted studies for flumetsulam.

Mutagenicity studies conducted with flumetsulam were negative. Flumetsulam did not alter the spontaneous tumor profile in these strains of rats and mice at the limit dose. Therefore, on the basis of the two studies, the Health Effects Division RfD/Peer Review Committee classified flumetsulam as a "Group E", evidence of non-carcinogenicity for humans (TXR# 011039, 03/24/1993).

Available metabolism and pharmacokinetics studies in mice and rats indicate that flumetsulam is primarily eliminated within 48 hours from all test animals following oral administration. The primary route was urinary excretion of unchanged flumetsulam. The rapid clearance of flumetsulam demonstrated little potential for bioaccumulation. Metabolic studies show that approximately 52-63% of the administered test material was absorbed by male and female rats. Plasma pharmacokinetic studies suggest that increased doses were associated with increased clearance, possibly due to saturation of plasma binding sites. In addition, there was a dose-

dependent decrease in the rate of plasma absorption and elimination for both rats and mice. Two very minor metabolites were detected in the urine of mice (not identified). At the limit dose, mice showed a greater capacity for absorption and elimination than rats.

### **3.2 Safety Factor for Infants and Children (FQPA Safety Factor)**

The flumetsulam risk assessment team has recommended that the FQPA Safety Factor be reduced to 1X based on adequate toxicity database and exposure data. There is no evidence of qualitative or quantitative susceptibility *in utero* or during post-natal exposure in developmental and reproduction studies and there is no evidence of neurotoxicity in the submitted studies. A developmental neurotoxicity study is not required since there was no evidence of neurotoxicity or neuropathy from the available studies.

#### **3.2.1 Completeness of the Toxicology Database**

The database for flumetsulam is complete and adequate to characterize potential pre- and/or post-natal risk for infants and children.

#### **3.2.2 Evidence of Neurotoxicity**

There are acute and subchronic neurotoxicity studies available. No evidence of neurotoxicity was observed in any of the submitted studies for flumetsulam. A developmental neurotoxicity study is not required.

#### **3.2.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal**

The available data do not provide evidence of any increased susceptibility or sensitivity in the offspring in either of the two developmental toxicity studies, nor in the two-generation reproduction study.

#### **3.2.4 Residual Uncertainty in the Exposure Database**

There are no residual uncertainties with regard to dietary exposure. Conservative, upper-bound assumptions were used to determine exposure through dietary sources (food and drinking water), such that these exposures have not been underestimated. There are currently no residential uses and no outstanding exposure data requirements for flumetsulam.

### **3.3 Toxicity Endpoint and Point of Departure Selections**

Previously, HED has conducted a comprehensive risk assessment for flumetsulam (E. Reeves and S. Ary, D306238, 11/22/2004). There have been no changes to the prior dose-response assessment and no changes to the prior recommendations for combining routes of exposure and/or cancer classification.

An acute reference dose has not been established for either the general population or for females 13-49 years of age since there were no appropriate studies that demonstrated evidence of toxicity attributable to a single dose for these populations. For chronic dietary and other exposure

scenarios, the chronic feeding study in the dog was selected because the study encompasses the appropriate exposure duration and provides a screening level hazard with a NOAEL of 100 mg/kg/day and LOAEL of 500 mg/kg/day based on renal inflammatory and atrophic changes secondary to renal calculi and hepatic effects consisting of inflammation, focal necrosis, and biliary stasis. For dermal exposure scenario, no systemic toxicity was found in the 21-day rabbit dermal study at the limit dose (1000 mg/kg/day). Quantification of dermal risk assessment is not required for this exposure due to lack of dermal, systemic, neuro, or developmental toxicity concerns. The detailed endpoint selection is listed in the following Table 3.3.

**Table 3.3 - Toxicological Doses and Endpoint for Use in Flumetsulam Dietary and Non-Occupational and Occupational Human Health Risk Assessments**

Exposure /Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (all populations)	An acute reference dose has not been established for either the general population or for females 13-49 years of age since there were no appropriate studies that demonstrated evidence of toxicity attributable to a single dose for these populations.			
Chronic Dietary (all populations)	NOAEL = 100 mg/kg/day	$UF_A = 10X$ $UF_H = 10X$ $FQPA\ SF = 1X$  Total UF = 100X	Chronic RfD = 1.0 mg/kg/day  $cPAD = \frac{\text{Chronic RfD}}{FQPA\ SF}$ = 1.0 mg/kg/day	<u>Chronic feeding study in dogs</u> LOAEL = 500 mg/kg/day based on renal inflammatory and atrophic changes secondary to renal calculi and hepatic effects (inflammation, focal necrosis, biliary stasis)
Incidental Oral (short and intermediated-term)	NOAEL = 100 mg/kg/day	$UF_A = 10X$ $UF_H = 10X$ $FQPA\ SF = 1X$	Residential LOC for MOE=100	Same as chronic dietary endpoint.
Dermal Exposure (all durations)	No hazard identified. No systemic toxicity was found in the 21-day rabbit dermal study at the limit dose (1000 mg/kg/day). Quantification of dermal risk assessment is not required for this exposure due to lack of dermal, systemic, neuro, or developmental toxicity concerns.			
Inhalation Exposure (all durations)	Oral NOAEL= 100 mg/kg/day (inhalation absorption rate = 100%)	$UF_A = 10X$ $UF_H = 10X$  Total UF = 100X	Occupational LOC for MOE = 100	Same as chronic dietary endpoint.
Cancer (oral, dermal, inhalation)	Flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans). Not mutagenic.			

UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic), RfD = reference dose, LOC = level of concern, NA = Not Applicable.  $UF_A$  = extrapolation from animal to human (interspecies),  $UF_H$  = potential variation in sensitivity among members of the human population (intraspecies).

### 3.4 Endocrine Disruption

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and

chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for flumetsulam, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), flumetsulam is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

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

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013<sup>1</sup> and includes flumetsulam. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.<sup>2</sup>

In the interim, EPA is making no human health or environmental safety findings associated with the EDSP screening of flumetsulam. Before completing this Registration Review, the Agency will make an EDSP FFDCA section 408(p) determination.

## **4.0 Dietary Exposure and Risk Assessment**

### **4.1 Degradate Residue Profile**

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<sup>1</sup> See <http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074> for the final second list of chemicals.

<sup>2</sup> <http://www.epa.gov/endo/>

#### 4.1.1 Summary of Environmental Degradation

Flumetsulam is classified as moderately persistent to persistent, and mobile to highly mobile in the environment. The environmental fate database for flumetsulam is largely complete.

Environmental fate studies show that flumetsulam is moderately persistent in soil (aerobic half-lives on the order of weeks to months), more persistent under anaerobic aquatic conditions (half-life of about 6 months) and aerobic aquatic conditions (half-life > 1 year), and stable to both hydrolysis and photolysis. However, the persistence and mobility of flumetsulam appear to be influenced by pH and organic carbon content. Flumetsulam has a low vapor pressure and Henry's Law constant, and its physical properties indicate a low potential for volatilization.

While flumetsulam is more soluble in neutral waters than in acidic water, it is very resistant to abiotic reactions (stable to hydrolysis, as well as photolysis in water and on soil). The major route of dissipation for flumetsulam is believed to be metabolism in aerobic soils, where metabolism half lives ranged from 13 days in sandy loam to 130 days in loam soil. Metabolites were less than 10% of applied radioactivity and were not identified. Metabolism in the aquatic environment is expected to be much slower, with a reported anaerobic aquatic half-life of 183 days and an estimated aerobic aquatic half-life greater than a year. Under anaerobic aquatic conditions flumetsulam is reduced to flumetsulam hydrate. Oxidation will cause a transformation back to flumetsulam.

Flumetsulam degrades to CO<sub>2</sub> with no significant accumulation of intermediate degradates, except for reduced flumetsulam hydrate [N-(2,6 difluorophenyl)-4,5,6,7-tetrahydro-5-hydroxy-5-methyl-(1,2,4)-triazolo(1,5-a)pyrimidine-2-sulfonamide], formed in the anaerobic aquatic study. Flumetsulam hydrate accounted for 52% of the total applied radiation at day 360, and degraded with a half life of about 180 days. However, this degradate was found to accumulate less (max of <8% of total applied radiation) and degrade more quickly (t<sub>1/2</sub> about 2 days) in a weakly anaerobic test system that became progressively more anaerobic with time. Flumetsulam degraded much slower in aerobic aquatic systems compared to anaerobic aquatic conditions. No degradation products were identified. Calculated pseudo-first order half-lives were 1762 and 1319 days for the <sup>14</sup>C-pyrimidine and <sup>14</sup>C-aniline labels, respectively.

Since flumetsulam does not rapidly metabolize when in contact with soils and does not bind strongly to soil surfaces, there is a potential for runoff from application sites to adjacent surface waters. Persistence in water indicates that flumetsulam may persist long enough to present some concern to surface water and ground water resources. Volatilization is not expected to be a major route of dissipation from either water or soil for flumetsulam.

EFED provided an updated drinking water assessment which estimated flumetsulam in surface and ground water based on the latest product label information, newly available environmental data, exposure models, and model scenarios.

#### 4.1.2 Residues of Concern Summary and Rationale

On April 21, 1993, the HED Metabolism Committee concluded that the residue of concern resulting from the uses of flumetsulam on plant commodities is flumetsulam only. The basis for



this decision was on the low levels of total radioactive residues present in plant metabolism studies and the lack of toxicological concern for metabolites having the sulfonamide linkage intact (N. Dodd, HED Metabolism Committee Memorandum, 04/26/1993).

The HED Metabolism Committee has not determined the residue of concern in livestock; however, based on the previously submitted data, the nature of the residue in livestock (goats and hens) is adequately defined; no detectable residues of flumetsulam were found in feed items.

<b>Table 4.1.2 Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression</b>			
Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Flumetsulam	Flumetsulam
Livestock	Ruminant	NA <sup>1</sup>	NA <sup>1</sup>
Drinking Water		Flumetsulam	Not Applicable

<sup>1</sup> HED previously concluded that there is no reasonable expectation of finite residues in ruminant and poultry commodities; i.e., 40 CFR §180.6(a)(3) situation.

### 4.1.3 Enforcement Analytical Method

The available analytical methodology (Gas Chromatography/Mass Spectrometry [GC/MS]) is considered adequate for tolerance enforcement of flumetsulam in/on plant commodities; DowElanco's Method ACR 91.6 (Method I) on soybean grain and DowElanco's Method ACR 91.61S (Method II) on corn grain and corn fodder (D189444, N. Dodd, 03/29/1993). The method has been submitted for inclusion in the Pesticide Analytical Manual (PAM), Volume II. The stated limit of quantitation (LOQ) of the method is 0.010 ppm; however, Analytical Bio-Chemistry Laboratories, Inc (ACB) validated the method LOQ at 0.05 ppm.

## 4.2 Food Residue Profile

### *Crop Field Trials*

Adequate crop field trial data are available for flumetsulam in/on field corn, soybean and dry beans. All flumetsulam residues were below the LOQ at the maximum label rate for all the registered crops. The established tolerances are at 0.05 ppm (40 CFR §180.468).

### *Meat, Milk, Poultry, and Eggs*

There are no registered direct livestock treatment uses for flumetsulam and no detectable residues of flumetsulam in/on the feed items except in soybean. However, for soybean, the registrant had proposed a tolerance for the soybean (bean) only and put grazing/feeding restrictions on the label; therefore, livestock analytical methods or feeding studies are not required (see memorandum by Dodd, N., "Issues to be Presented at the 4/21/93 Meeting of the HED Metabolism Committee."). Restriction on soybean feed items for livestock consumption should be on all labels. Nature of residue studies for ruminant (goat) and poultry (hens) have been submitted and reviewed. The nature of the residue in animals is adequate for the current uses. HED previously concluded that the registered uses on corn, soybeans, and dry beans results in a 40 CFR §180.6(a)(3) situation for ruminant and poultry commodities; i.e., there is no

reasonable expectation of finite residues in ruminant and poultry commodities. Therefore, additional data on the transfer of residues to meat, milk, and poultry are not required. However, for any future uses which may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required. Such data may, in turn, trigger the need for magnitude of the residue (feeding) studies in livestock.

#### *Processed Food and Feed*

Processing studies for the currently registered flumetsulam uses are adequate. Flumetsulam processing studies are available for corn. Flumetsulam residues in the treated corn at exaggerated maximum application rate and in the processed fractions were non-detects. A processing study is not required for soybeans as no detectable residues were found in soybeans from exaggerated application rate (D188957, N. Dodd, 06/28/1993) and (PP# 1G4006, N. Dodd, 03/27/1993).

#### *Storage Stability*

Storage stability studies using fortified samples of field corn and soybean for the currently registered flumetsulam uses are adequate. The results indicate that residues of flumetsulam are stable in corn grain, forage, and fodder stored for at least 555 days and in soybean for at up to thirty months (908 days) at -15 °C (N. Dodd, PP# 3F4185, 06/28/1993, and PP# 2F4036, 04/14/1993). For dry beans, in the absence of specific storage stability data, it was assumed that residues on samples which were stored for 97 days will behave similarly in beans as in corn and soybeans S. Ary (D306242, 08/31/2004).

#### *Rotational Crops*

The current use labels for flumetsulam restricts crop rotation after treatment to four months or greater for all crops except soybean.

### **4.3 Water Residue Profile**

Flumetsulam is soluble in water and is stable under photolysis. Degradation studies indicate the soil half-life ranges from approximately two weeks to four months with majority degrading in less than two months (mean of 69.5 days). The Environmental Fate and Effects Division (EFED) provided estimated drinking water concentrations (EDWCs) by using either a Tier I Screening Concentration In Ground Water (SCI-GROW) and/or Pesticide Root Zone Model – Ground Water (PRZM-GW) models for ground water; Tier II Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) was used to obtain surface water concentrations. The estimated 1-in-10 year annual mean residue of flumetsulam for chronic surface water using PRZM/EXAMS was 1.45 ppb, based on application on the Kansas corn scenario. The estimated flumetsulam residue using PRZM-GW model for chronic ground water EDWC was 14.8 ppb (J. Wolf, D411277, 8/16/2013).

**Table 4.3 - Maximum Flumetsulam EDWCs for Corn scenario in Surface Water and Groundwater**

Drinking Water Source (Model)	1-in-10 year		30 - year Average	30 - year Simulation	
	Acute	Chronic	Cancer	Acute	Chronic
	(µg/L/ppb)				
Surface Water (PRZM/EXAMS)	6.68	1.45	0.76	-	-
Groundwater (PRZM-GW)	-	-	-	19.8	14.8

#### 4.4 Dietary Risk Assessment

An aggregate dietary food and drinking water, exposure and risk assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16. This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The analysis also incorporated the highest estimated flumetsulam residue in water provided by EFED. In a chronic dietary risk assessment, risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). The population-adjusted chronic dose or cPAD is equivalent to the reference dose (RfD) divided by the Food Quality Protection Act (FQPA) Safety Factor. Dietary risk assessments incorporates both exposure and toxicity data for a given pesticide.

##### 4.4.1 Description of Residue Data Used in Dietary Assessment

Tolerance-level residues were used for all registered commodities in the unrefined chronic aggregate dietary analysis for flumetsulam. For drinking water, the highest estimated chronic drinking water concentration of 14.8 ppb from ground water sources was used.

##### 4.4.2 Percent Crop Treated Used in Dietary Assessment

It was assumed that 100% of the registered crops were treated (100%CT) in the unrefined chronic aggregate dietary analysis for flumetsulam.

##### 4.4.3 Acute Dietary Risk Assessment

Since no appropriate endpoints were identified from the available flumetsulam toxicity studies, an acute dietary exposure risk assessment is not required.

##### 4.4.4 Chronic Dietary Risk Assessment

The chronic dietary exposure analysis results for the general U.S. population, all infants (less than 1 year old), children 1-2, children 3- 5, children 6-12, youth 13-19, females 13-49, adults

20-49, and adults 50-99 years. The resulting food exposure estimates are below HED's level of concern for the U.S. population and all population subgroups at less than 1% of cPAD.

#### 4.4.5 Cancer Dietary Risk Assessment

Since flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans), no cancer dietary risk exposure risk assessment is required.

#### 4.4.6 Dietary Risk Assessment Summary Table

<b>Table 4.4.6. Summary of Dietary (Food and Drinking) Exposure and Risk for Flumetsulam.</b>						
<b>Population Subgroup</b>	<b>Acute Dietary</b>		<b>Chronic Dietary</b>		<b>Cancer</b>	
	<b>Dietary Exposure (mg/kg/day)</b>	<b>% aPAD</b>	<b>Dietary Exposure (mg/kg/day)</b>	<b>% cPAD</b>	<b>Dietary Exposure (mg/kg/day)</b>	<b>Risk</b>
General U.S. Population	N/A	N/A	0.000435	< 1	N/A	N/A
All Infants (<1 year old)			0.001007			
Children 1-2 years old			0.000735			
Children 3-5 years old			0.000665			
Children 6-12 years old			0.000481			
Youth 13-19 years old			0.000372			
Adults 20-49 years old			0.000420			
Adults 50-99 years old			0.000376			
Females 13-49 years old			0.000412			

### 5.0 Residential (Non-Occupational) Exposure/Risk Characterization

There are currently no registered residential uses associated with flumetsulam. Any future proposed residential uses could impact the human health aggregate risk assessment for flumetsulam.

#### 5.1 Spray Drift

Off-target movement of pesticides can occur via many types of pathways and it is governed by a variety of factors. Sprays that are released and do not deposit in the application area end up off-

target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to exposures (e.g., children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling coupled with methods employed for residential risk assessments for turf products.

The approach to be used for quantitatively incorporating spray drift into risk assessment include assessing exposures for children (1 to 2 years old) and adults who have contact with turf where residues are assumed to have deposited via spray drift thus resulting in an exposure scenario. Aside from the predicted residues available for transfer, the routes of exposure and assessment methodology is analogous to how exposures to turf products are considered in risk assessment.

In order to evaluate the drift potential and associated risks, an approach based on drift modeling coupled with techniques used to evaluate residential uses of pesticides was utilized. Essentially, a residential turf assessment based on exposure to deposited residues has been completed to address drift from the agricultural applications of flumetsulam. In the spray drift scenario, the deposited residue value was determined based on the amount of spray drift that may occur at varying distances from the edge of the treated field using the AgDrift (v2.1.1) model. *Exposures were considered for 50 feet wide lawns where the nearest side of the property was directly adjoining the treated field (at field edge) and at varied distances up to 300 feet downwind of a treated field.* Once the deposited residue values were determined, the remainder of the spray drift assessment was based on the algorithms and input values specified in the recently revised (2012) *Standard Operating Procedures For Residential Risk Assessment (SOPs)*.

A screening approach was developed for situations where specific label guidance for application parameters is not available.<sup>3</sup> AgDrift is appropriate for use only when applications are made by aircraft, airblast sprayers, and groundboom sprayers. When AgDrift was developed, a series of screening values (i.e., the Tier 1 option) were incorporated into the model and represent each equipment type and use under varied conditions. The screening options specifically recommended in this methodology were selected because they are plausible and represent a reasonable upper bound level of drift for common application methods in agriculture. In all cases, each scenario is to be evaluated unless it is not plausible based on the anticipated use pattern (e.g., herbicides are not typically applied to tree canopies) or specific label prohibitions (e.g., aerial applications are not allowed).

The spray drift risk estimates are based on an estimated deposited residue concentration as a result of the screening level agricultural application scenarios. Flumetsulam is used on soybeans field corn, and dry beans. The chemical can be applied via groundboom and for field corn and soybeans by aerial equipment. The recommended drift scenario screening level options are listed below:

- Groundboom applications are based on the AgDrift option for high boom height and using very fine to fine spray type using the 90<sup>th</sup> percentile results.

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<sup>3</sup> Note that for many cases the scenarios outlined in the screening approach represent actual use practice.

- Aerial applications are based on the use of AgDrift Tier 1 aerial option for a fine to medium spray type and a series of other parameters which will be described in more detail below (e.g., wind vector assumed to be 10 mph in a downwind direction for entire application/drift event).

There are no dermal endpoints selected for flumetsulam, therefore adult and children (1<2 years old) dermal spray drift exposure was not assessed. However the HtM exposure for children 1<2 years old was assessed using the incidental oral endpoint from a chronic oral dog study with an oral NOAEL of 100 mg/kg/day. The total applicable Level of Concern is 100 so MOEs < 100 would be of concern.

Results are presented in Table 1: Appendix D, “Residential Exposure to Flumetsulam from Agricultural Drift for Children Ages 1<2 years Hand to Mouth, HtM only.” The spray drift risk estimates indicate that there are no major risk concerns from aerial and ground boom applications to field corn, and soybeans from field edge. In addition there are also no major spray drift risk concerns for the ground application to flumetsulam to dry beans from field edge. All MOE estimates were  $\geq 100$  and ranged from 370,000 to 4,000,000 at edge. Risk estimates for the varying flumetsulam product formulations, (i.e. water dispersible granular and emulsifiable concentrate) were below the level of concern, MOEs <100. The risk can be even further reduced by changing nozzle types with coarser sprays resulting in less drift.

## 5.2 Inhalation Post-application Exposure

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for flumetsulam at this time primarily because of the low acute inhalation toxicity (Toxicity Category III and IV), low vapor pressure  $1.0 \times 10^{-15}$  mm HG @ 25° C, and the low proposed use rate (0.05 lb ai/A and 0.07 lb ai/A). However, volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010<sup>4</sup>. The Agency is in the process of evaluating the SAP report and may, as appropriate, develop policies and procedures to identify the need for and, subsequently, the way to incorporate post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are developed, the Agency may revisit the need for a quantitative post-application inhalation exposure assessment for flumetsulam.

An inhalation exposure assessment was performed for flaggers exposed from aerial application of flumetsulam. This exposure scenario is representative of a worse case inhalation (drift) exposure and may be considered protective of most outdoor agricultural and commercial post-application inhalation exposure scenarios. The estimated MOE for flaggers is 930,000 which is well above the margin of concern of 100; i.e., not a risk concern.

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<sup>4</sup> Available: <http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html>

## **6.0 Aggregate Exposure/Risk Characterization**

Aggregate risk assessments evaluate the combined risk from dietary exposure (food and water) and any non-occupational (residential) uses. There are currently no registered residential uses associated with flumetsulam; therefore, a residential/non-occupational exposure assessment is not required. As a result, the flumetsulam aggregate risk assessment includes only dietary exposure (food and water). An acute dietary exposure assessment was not performed as no appropriate endpoints were identified from the available flumetsulam toxicity studies for the acute dietary scenario. The chronic dietary exposure estimates from food and drinking water do not exceed HED's level of concern. A cancer dietary exposure assessment was not performed as flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans). Sections 4.4.4 and 4.4.5 discuss the chronic and dietary (food and water) exposure assessments.

## **7.0 Cumulative Exposure/Risk Characterization**

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to flumetsulam and any other substances. For the purposes of this assessment, therefore, EPA has not assumed that flumetsulam has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

## **8.0 Occupational Exposure/Risk Characterization**

Flumetsulam is currently registered on field corn, soybean and dry bean by ground and aerial applications (see Table 2.3). Based on the existing use pattern for flumetsulam, there is potential for both occupational handler and occupational post-application exposure to occur. There is a potential for agricultural handlers and post-application workers to have dermal exposure to flumetsulam during the course of typical agricultural activities. However, quantification of dermal risk assessment is not required for this exposure due to lack of dermal, systemic, neuro, or developmental toxicity concerns. Therefore, only inhalation exposure was assessed for handlers.

### **8.1 Occupational Handler Exposure and Risk**

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the currently registered use patterns and types of equipment and techniques that can potentially be used, occupational handler exposure is expected for flumetsulam. The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios:

- 1) Mixing/loading water dispersible granular (WDG) for groundboom application,
- 2) Mixing/loading WDG for aerial application,
- 3) Mixing/loading water soluble packet (WSP) for groundboom application,
- 4) Mixing/loading WSP for aerial application,
- 5) Mixing/loading emulsifiable concentrate for ground application,
- 6) Impregnating dry bulk fertilizer with EC, WDG, and WSP formulations.
- 7) Applying liquid spray with a groundboom,
- 8) Applying liquid spray with aerial application; and
- 9) Flagger scenario.

Field corn, soybeans, and dry beans are considered to be high acreage crops and it is unlikely that a farmer would apply the chemical with handheld equipment because of acreage size. Therefore, the handheld equipment scenario was not included in this assessment.

For impregnation of dry bulk fertilizer, the product labels provide the amount of product to be applied to a ton of fertilizer based on the pounds of fertilizer used per acre and amount of product recommended per acre. Flumetsulam labels require a minimum of 200 pounds of dry fertilizer per acre multiplied by the label rate per acre with a conversion fact of 2000 lbs per ton. HED does not have data regarding the mixing/loading or the application of flumetsulam impregnated dry bulk fertilizer. Additionally, HED does not have scenario specific exposure data for impregnated dry bulk fertilizer. However, a mixing and loading processing rate of dry bulk fertilizer has been calculated to be 960 tons of fertilizer processed per 8 hour day. This rate was supplied by a registrant concerning the chemical alachlor and is referenced in the RED document D330812. The processing rate and label specific information specifying a closed system for impregnating the fertilizer with flumetsulam was achieved using this exposure surrogate data. HED assumed closed mixing/loading for commercial applications as the exposure scenario. On-farm application was then assessed using an open cab spreader as surrogate data with 320 acres/day for commercial equipment.

It is the policy of HED to use the best available data to assess handler exposure. Sources of generic occupational handler data, used as surrogate data in the absence of chemical-specific data, include the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1), the Agricultural Handler Exposure Task Force (AHETF) database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data) and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting occupational handler exposure that are used in this assessment, known as “unit exposures”, are outlined in the “Occupational Pesticide Handler Unit Exposure Surrogate Reference Table” (<http://www.epa.gov/opp00001/science/handler-exposure-table.pdf>), which, along with



additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at <http://www.epa.gov/pesticides/science/handler-exposure-data.html>.

### **8.1.1 Short-/Intermediate-Term Non-Cancer Handler Exposure and Risk**

HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. For flumetsulam based on the use pattern for application to field corn and soybeans, and dry beans short-term exposure is expected however it is possible that large agribusiness or commercial applicators could apply flumetsulam over a period of weeks. Therefore intermediate exposure could be expected as well. The same endpoints were selected for short-term and long term exposure. Long-term exposures are not expected; therefore, a long-term assessment was not conducted.

Short- and intermediate-term occupational handler exposure and risks were estimated using 1) unit exposures taken from the “Occupational Pesticide Handler Unit Exposure Surrogate Reference Table”; 2) the maximum flumetsulam label application rates; and 3) amount handled/area treated values take from ExpoSAC SOP No. 9.1, “Standard Values for Daily Acres Treated in Agriculture”.

There is a potential for agricultural handlers and post-application workers to have dermal exposure to flumetsulam during the course of typical agricultural activities. However, there is no hazard identified for dermal exposure. Therefore, only inhalation exposure was assessed for handlers.

Table 8.1.1 presents the estimated inhalation occupational handler risk estimates for the currently registered uses of flumetsulam at baseline personal protective equipment (PPE). Baselines PPE is defined as a single layer of clothing consisting of a long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator. The short- and intermediate-term risk estimates for all occupational handler scenarios do not exceed HED’s level of concern (MOEs > 100). The occupational handler inhalation risk estimates range from 11,000 to 19,000,000. HED notes that current flumetsulam labels require PPE consisting of a long-sleeved shirt, long pants, shoes plus socks, and pair of chemical-resistant gloves for all applicators and other handlers.

**Table 8.1.1 - Occupational Handler Non-Cancer Exposure and Risk Estimates for Flumetsulam Use on Field Corn and Soybeans at Baseline<sup>1</sup>**

Exposure Scenario	Crop	Inhalation Unit Exposure (µg/lb ai) <sup>2</sup>	Maximum Application Rate <sup>3</sup>	Area Treated or Amount Handled Daily <sup>4</sup>	Inhalation	
		Mitigation Level			Dose (mg/kg/day) <sup>5</sup>	MOE <sup>6</sup>
Mixer/Loader						
Aerial Water Dispersible Granular	Field Corn and Soybeans	8.96 No Respirator	0.07 lb a.i./acre	1200 acres	0.0094	11,000
Aerial Water Soluble Packet <sup>7</sup>	Field Corn and Soybeans	0.24 EC		0.7 lb ai/ton of fertilizer	0.0003	400,000
Ground Water Soluble Pack <sup>7</sup> impregnating fertilizer		0.24 EC Closed System	960 tons of fertilizer		0.00201	50,000
Ground Water Dispersible Granular impregnating fertilizer						
Ground Emulsifiable Concentrate impregnating fertilizer	Field Corn	0.083 EC Closed System	0.05 lb a.i./acre	200 acres	0.0005	200,000
Ground Emulsifiable Concentrate		0.219 No Respirator	0.5 lb a.i./ton of fertilizer		0.00003	3,600,000
Ground Water Dispersible Granular	Field Corn and Soybeans	8.96 No Respirator	0.07 lb a.i./acre	200 acres	0.0016	64,000
Ground Water Soluble Packet		0.24 EC			0.00004	2,400,000
Ground Emulsifiable Concentrate impregnating fertilizer	Dry beans <sup>10</sup>	0.083 EC Closed System	0.07 lb a.i./acre	960 tons of fertilizer	0.0007	140,000
Ground Emulsifiable Concentrate		0.219 No Respirator	0.7 lb a.i./ton of fertilizer	200 acres	0.00004	2,600,000
Ground Water Dispersible Granular		8.96 No Respirator			0.0016	64,000

**Table 8.1.1 - Occupational Handler Non-Cancer Exposure and Risk Estimates for Flumetsulam Use on Field Corn and Soybeans at Baseline<sup>1</sup>**

Exposure Scenario	Crop	Inhalation Unit Exposure (µg/lb ai) <sup>2</sup>	Maximum Application Rate <sup>3</sup>	Area Treated or Amount Handled Daily <sup>4</sup>	Inhalation	
		Mitigation Level			Dose (mg/kg/day) <sup>5</sup>	MOE <sup>6</sup>
Applicator						
Aerial <sup>8</sup> Water Dispersible Granular within a Water Soluble Packet	Field Corn and Soybeans	0.0049 EC Closed Cockpit	0.07 lb a.i./acre	1200	.0000052	19,000,000
Ground Water Dispersible Granular and Water Dispersible Granular within a Water Soluble Packet	Field Corn, Soybeans, and Dry Beans	0.34 No Respirator		200	0.00006	1,700,000
Ground Emulsifiable Concentrate	Field Corn s				0.00004	2,400,000
	Dry Beans				0.00006	1,700,000
Impregnated Fertilizer <sup>9</sup> Tractor drawn spreader	Field Corn, Soybeans, Dry Beans	1.2 No Respirator	0.07 lb a.i./acre	360 acres	0.00034	300,000
Impregnated Fertilizer <sup>9</sup> Tractor drawn spreader	Field Corn and Soybeans		0.05 lb a.i./acre	360 acres	0.00024	420,000
Flagger						
Sprays Water Dispersible Granular within a Water Soluble Packet	Field Corn, and Soybeans	0.35 No Respirator	0.07 lb a.i./acre	350	0.00011	930,000

<sup>1</sup> Baseline PPE includes long sleeved pants, long sleeved shirt, shoes and sock and no respirator.

<sup>2</sup> Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table; Level of mitigation: No respirator, EC = Engineering Controls

<sup>3</sup> Based on registered or proposed labels for flumetsulam. See Profile Table 4.1

<sup>4</sup> Exposure Science Advisory Council Policy #9.1.

<sup>5</sup> Inhalation Dose = Inhalation Unit Exposure ( $\mu\text{g/lb ai}$ )  $\times$  Conversion Factor (0.001  $\text{mg}/\mu\text{g}$ )  $\times$  Application Rate (lb ai/acre)  $\times$  Area Treated or Amount Handled Daily (A)  $\div$  BW (kg).

<sup>6</sup> Inhalation MOE = Inhalation NOAEL ( $\text{mg/kg/day}$ )  $\div$  Inhalation Dose ( $\text{mg/kg/day}$ ).

<sup>7</sup> Water Soluble Packets, or WSPs are considered an engineering control. Unit exposures for chemicals packaged this way are lower than baseline which assumes no respirator

<sup>8</sup> Aerial application is assumed to be done with closed cockpit which is considered an engineered control not baseline protection.

<sup>9</sup> EPA reg number 62719-570 label notates for impregnating fertilizer use a minimum of 200 lb of dry bulk fertilizer per acre with maximum of 3 pints of product per acre.

<sup>10</sup> Dry Bean use scenarios and application rates based on inactive registration numbers and 2004 memo D306178.

### **8.1.2 Cancer Handler Exposure and Risk**

A cancer handler exposure and risk assessment was not performed as flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans).

## **8.2 Occupational Post-Application Exposure and Risk**

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

### **8.2.1 Post-application Inhalation Exposure**

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for flumetsulam at this time primarily because of the low acute inhalation toxicity (Toxicity Category III and IV), low vapor pressure  $1.0 \times 10^{-15}$  mm HG @ 25°C, and the low proposed use rates (0.07 and 0.5 lb ai/A). However, there are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010<sup>5</sup>. The Agency is in the process of evaluating the SAP report as well as available post-application inhalation exposure data generated by the Agricultural Reentry Task Force and may, as appropriate, develop policies and procedures, to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for flumetsulam.

Although a quantitative post-application inhalation exposure assessment was not performed, an inhalation exposure assessment was performed for occupational/commercial handlers. Handler exposure resulting from application of pesticides outdoors is likely to result in higher exposure than post-application exposure. Therefore, it is expected that these handler inhalation exposure estimates would be protective of most occupational post-application inhalation exposure scenarios.

### **8.2.2 Post-application Dermal Exposure and Risk**

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<sup>5</sup> Available: <http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html>

### **8.2.2.1 Short-/Intermediate-Term Non-Cancer Post-application Exposure and Risk**

A quantitative occupational post application dermal exposure assessment was not performed due to lack of dermal endpoint selection.

#### Restricted Entry Interval

The REI specified on the proposed label is based on the acute toxicity of flumetsulam. Flumetsulam is classified as Toxicity Category III or IV via the dermal route and skin irritation potential. It is not a skin sensitizer. Short- and intermediate-term post-application risk estimates were not a concern on day 0 (12 hours following application) for all post-application activities. Under 40 CFR 156.208 (c) (2) (iii), active ingredients classified as Acute III or IV for acute dermal, eye irritation and primary skin irritation are assigned a 12-hour REI. Therefore, the [156 subpart K] Worker Protection Statement interim REI of 12 hours is adequate to protect agricultural workers from post-application exposures to flumetsulam. Products that include a formulated mixture of active ingredient should retain the 48 hour REI.

### **8.2.2.2 Cancer Post-application Exposure and Risk**

A cancer post-application exposure and risk assessment was not performed as flumetsulam is classified as Group E (Evidence of non-carcinogenicity for humans).

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## Appendix A. Toxicology Assessment

### A.1 Toxicology Data Requirements

The requirements (40CFR §158.340) for food use of flumetsulam are in Table A.1.

TABLE A.1 - Toxicology Data Requirements for Flumetsulam		
Study	Technical	
	Required	Satisfied
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Primary Eye Irritation	yes	yes
870.2500 Primary Dermal Irritation	yes	yes
870.2600 Dermal Sensitization	yes	yes
870.3100 Oral Subchronic (rodent)	yes	yes
870.3150 Oral Subchronic (non-rodent)	yes	yes
870.3200 21/28-Day Dermal	yes	yes
870.3250 90-Day Dermal	no	no
870.3465 90-Day Inhalation	yes	yes <sup>a</sup>
870.3700a Developmental Toxicity (rodent)	yes	yes
870.3700b Developmental Toxicity (non-rodent)	yes	yes
870.3800 Reproduction	yes	yes
870.4100a Chronic Toxicity (rodent)	yes	yes
870.4100b Chronic Toxicity (non-rodent)	yes	yes
870.4200a Oncogenicity (rat)	yes	yes
870.4200b Oncogenicity (mouse)	yes	yes
870.4300 Chronic/Oncogenicity	yes	yes
870.5100 Mutagenicity—Gene Mutation (bacterial)	yes	yes
870.5300 Mutagenicity—Gene Mutation (mammalian)	yes	yes
870.5375 Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5395 Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a Acute Delayed Neurotoxicity (hen)	no	no
870.6100b 90-Day Neurotoxicity (hen)	no	no
870.6200a Acute Neurotoxicity Screening Battery (rat)	yes	yes
870.6200b 90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300 Developmental Neurotoxicity	no	no
870.7485 General Metabolism	yes	yes
870.7600 Dermal Penetration	no	no
870.7800 Immunotoxicity	yes	yes

<sup>a</sup>Inhalation study is waived by the HASPOC.



## A.2 Toxicity Profile

**TABLE A.2.1 - Acute Toxicity Profile for Flumetsulam**

Guideline Number	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral [Rat]	41263202	LD <sub>50</sub> >5000 mg/kg (M/F)	IV
870.1200	Acute dermal [Rabbit]	41263203	LD <sub>50</sub> >2000 mg/kg (M/F)	III
870.1300	Acute inhalation [Rat]	41556501	LC <sub>50</sub> >0.65 mg/L (M/F)	IV
870.2400	Acute eye irritation [Rabbit]	41263204	Slight conjunctival reddening and chemosis and iridal redness at 1 hour	IV
870.2500	Acute dermal irritation [Rabbit]	41263205	Not an irritant	IV
870.2600	Skin sensitization [Guinea pig]	41263206	Not a skin sensitizer	NA

**TABLE A.2.2 - Subchronic, Chronic, and other Toxicity Profile for Flumetsulam**

Guideline Number/ Study Type	MRIDs/Year/Doses Classification	Results
870.3100 90-Day oral toxicity, Rat	41263212 (1988) 0, 250, 1000, 2000/2500 mg/kg/day Acceptable/Guideline	NOAEL (M/F) 250 mg/kg/day LOAEL (M/F) 1000 mg/kg/day based on severe bilateral tubular-interstitial nephritis.
870.3100 90-Day oral toxicity, Mice	41931704 (1987) 0, 100, 500, 1000, 5000 mg/kg/day Acceptable/Guideline	NOAEL (M/F) 5000 mg/kg/day (98.6% a.i.) LOAEL (M/F) Not identified. Statistically increased full cecum weights and decreased kidney weights were found at 5000 mg/kg/day but were considered adaptive and/or toxicologically irrelevant.
870.3200 21-Day Dermal, Rabbit	41931706 (1990) 0, 100, 500, 1000 mg/kg/day Acceptable/Guideline	Systemic & dermal NOAEL (M/F) >1000 mg/kg/day. LOAEL (M/F) Not identified Diffuse treatment-related epidermal hyperplasia observed at application site.
870.3700a Developmental Toxicity, Rat (GD 6-15)	41263213, 41615301 (1990) 0, 100, 500, 1000, mg/kg/day Acceptable/Guideline	Maternal NOAEL 500 mg/kg/day Maternal LOAEL 1000 mg/kg/day, based on statistically increased full cecum weights and decreased kidney weights, but considered adaptive and/or toxicologically irrelevant. Developmental NOAEL >1000 mg/kg/day Developmental LOAEL Not identified. No developmental toxicity reported.
870.3700b Developmental Toxicity, Rabbit (GD 7-19)	41931709 (1989) 0, 100, 500, 700 mg/kg/day Acceptable/Guideline	Maternal NOAEL=100 mg/kg/day Maternal LOAEL= 500 mg/kg/day based on anorexia, moribundity, and decreased body weight gain (GD 10-13 at 500 and GD 7-10 at 700 mg/kg/day) Developmental NOAEL> 700 mg/kg/day Developmental LOAEL= Not identified
870.3800 Reproduction (2-	41931710 (42474001) (1990) 0, 100, 500, 1000	Reproductive NOAEL >1000 mg/kg/day Reproductive LOAEL Not identified Offspring NOAEL > 1000 mg/kg/day

<b>TABLE A.2.2 - Subchronic, Chronic, and other Toxicity Profile for Flumetsulam</b>		
<b>Guideline Number/ Study Type</b>	<b>MRIDs/Year/Doses Classification</b>	<b>Results</b>
Generation), Rat	mg/kg/day Acceptable/Guideline	Offspring LOAEL Not identified Parental NOAEL >1000 mg/kg/day Parental LOAEL Not identified
870.4100b Chronic Feeding, Dog	41952103 (1991) 0, 20, 100, 500 mg/kg/day Acceptable/Guideline	Systemic NOAEL (M) = 100 mg/kg/day Systemic NOAEL (F) >500 mg/kg/day Systemic LOAEL (M) = 500 mg/kg/day based on renal inflammatory and atrophic changes secondary to renal calculi and hepatic effects consisting of inflammation, focal necrosis, and biliary stasis LOAEL (F) Not identified
870.4200b Carcinogenicity, Mouse	41931708 (1991) 0, 100, 500, 1000 mg/kg/day Acceptable/Guideline	Systemic NOAEL (M/F) > 1000 mg/kg/day LOAEL (M/F) Not identified Not evidence for carcinogenicity in M/F
870.4300 Chronic/Oncogenicity, 2- Year- Rat	41931707 (1991) 0, 100, 500, 1000 mg/kg/day Acceptable/Guideline	NOAEL (M) = 500 mg/kg/day NOAEL (F) > 1000 mg/kg/day LOAEL (M) = 1000 mg/kg/day based on dilated renal pelvises containing renal calculi, atrophy of renal papillae, renal pelvic epithelial hyperplasia, and mineralization of pelvic epithelium LOAEL (F) Not identified Not evidence for carcinogenicity in M/F
870.5100 Ames bacterial mutagenicity test	41263214 (1988) Acceptable/Guideline	Salmonella - Negative in strains TA98, TA100, TA1535, TA1537, and TA1538 with and without metabolic activation at concentrations of 0.01-1.0 mg/plate
870.5300 In vitro mammalian cell gene mutation test (Chinese hamster ovary cells)	41263217 (1988) Acceptable/Guideline	The study was negative at concentrations from 500 to 3000 µg/mL with and without metabolic activation with Arochlor 1254 induced rat liver S-9
870.5395 <i>In Vivo</i> Micronucleus Assay	41263216 (1988) Acceptable/Guideline	Negative for micronucleus induction in bone marrow cells of male and female CD-1 mice at 24 hrs after oral gavage administration of 500 to 5000 mg/kg.
870.5550 Unscheduled DNA Synthesis	41263215 (1988) Acceptable/Guideline	Negative at concentrations from $3.16 \times 10^{-6}$ to $3.16 \times 10^{-4}$ M
870.7485 General Metabolism, Rat and Mouse	41931711 (1991) 41993801 (1988) Acceptable/Guideline	Absorbed test material (52-63%) excreted unchanged in urine. Unabsorbed test material eliminated unchanged in feces. Test material essentially eliminated within 48 hours by male and female rats. Plasma $^{14}\text{C}$ exhibited a dose-dependent increase in absorption and elimination. Increasing dose associated with increasing clearance possibly due to saturation of plasma binding sites. Male mice exhibited faster absorption and elimination at 1000

<b>TABLE A.2.2 - Subchronic, Chronic, and other Toxicity Profile for Flumetsulam</b>		
<b>Guideline Number/ Study Type</b>	<b>MRIDs/Year/Doses Classification</b>	<b>Results</b>
		mg/kg than male rats. Urine primary elimination route in both male and female rats and mice. Two minor metabolites identified in urine in mice.
870.6200 Acute Neurotoxicity Rat	48297902 (2009) 0,250,1000, 2000 mg/kg Acceptable/Guideline	Systemic/neurotoxicity NOAEL=2000 mg/kg No evidence of neurotoxicity
870.6200 Subchronic Neurotoxicity Rat	48798101 (2012) 0, 100, 300, 1000 mg/kg/day Acceptable/Guideline	Systemic/neurotoxicity NOAEL=1000 mg/kg/day No evidence of neurotoxicity.
870.7800 Immunotoxicity Rat	48694401 (2011) 0, 1000 mg/kg/day Acceptable/Guideline	Systemic/Immunotoxicity NOAEL=1000 mg/kg/day No evidence of immunotoxicity

## Appendix B. Physical/Chemical Properties

<b>Table B.1- Physicochemical Properties of the Technical Grade Test Compound Flumetsulam.</b>		
Parameter	Value	Reference /Comment
Melting point	252.9 °C	N. Dodd, PP# 1G4006, 03/27/1992
pH	3.44 at 24.4 °C for a 10% suspension in water	
Density	1.77 g/cm <sup>3</sup> at 21°C	
Water solubility	49.1 ± 0.5 mg/L at 25 °C, pH 2.5 5.65 ± 0.01 g/L at 25 °C, pH 7.0	
Solvent solubility (g/L)	17.0 g/L in acetone	N. Dodd, PP# 2F4036, 04/14/1993
	5.2 g/L in acetonitrile	
	0.0016 g/L in aromatic 100	
	9.0 g/L in cyclohexanone	
	261.0 g/L in dimethylformamide	
	Less than 0.001 g/L in hexane	
	3.3 g/L in methanol	
	Less than 0.001 g/L in o-xylene	
	0.06 g/L in octanol	
	11.0 g/L in tetrahydrofuran	
Vapor pressure	1.0 x 10 <sup>-15</sup> mm Hg at 25 °C	N. Dodd, PP# 1G4006, 03/27/1992
Dissociation constant	pK <sub>a</sub> = 4.6	
Octanol/water partition coefficient Log(K <sub>OW</sub> )	log P = 0.21	
Henry's Law Constant (25 °C)	6.14e <sup>-15</sup> atm-m <sup>3</sup> /mol @25 °C	Calculated
Aerobic Soil Metabolism Half-life (ASM) (T <sub>1/2</sub> )	<b>93</b> , 48, 47, 30, <b>23</b> , 44, 88, 36,19, 81,51,28, 44, 130, 13, 17, 20, 46, <b>60</b> , 59, <b>102</b> days [range 13 to 130 days; mean = 51.0 days]	T <sub>1/2</sub> identified in the problem formulation 23, 60, 93, 102 days; mean = 69,5 days (MRID 41263230).
Anaerobic Aquatic Soil Metabolism	183 days	
Aerobic Aquatic Metabolism Half-life (days)	1762 [ <sup>14</sup> C-pyrimidine ring] days 1319 [ <sup>14</sup> C-aniline ring] days	Studied reviewed but DER has not been completed by EFED.

**Appendix C. Review of Human Research**

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These studies, which comprise the Pesticide Handlers Exposure Database (PHED), the Outdoor Residential Exposure Task Force (ORETF) Database, the Agricultural Handler Exposure Task Force (AHETF), and the Agricultural Reentry Task Force (ARTF) have been determined to require a review of their ethical conduct, have received that review, and have been determined to be ethically conducted.

## Appendix D. Occupational Exposure/Risk Summary Tables

Table D.1- Residential Exposure to Flumetsulam from Agricultural Drift for Children Ages 1<2 years Hand to Mouth, HtM only														
Crop/Rate Group	Spray Type/ Nozzle Configuration	Application Rate (lb ai/A)	Estimated or Adjusted TTR <sub>i</sub> (ug/cm2)	At Edge	10 Feet	25 Feet	50 Feet	75 Feet	100 Feet	125 Feet	150 Feet	200 Feet	250 Feet	300 Feet
				HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE	HtM MOE
Soybeans, Field Corn, and Dry Beans <sup>1</sup>														
Aerial	<i>Fine to Medium</i>	0.07	0.0077805	370000	450000	560000	730000	960000	1200000	1500000	1700000	2300000	2800000	3400000
	Medium to Coarse			440000	600000	820000	1100000	1600000	2100000	2700000	3200000	4500000	5900000	7200000
	Coarse to Very Coarse			510000	760000	1100000	1800000	2500000	3400000	4300000	5200000	7200000	9400000	12000000
	Very Fine to Fine			250000	280000	310000	360000	420000	480000	540000	610000	740000	870000	990000
	AT401, M, 10 mph, 37% SD			400000	510000	660000	890000	1200000	1600000	1900000	2200000	2900000	3600000	4500000
	WASP, M, 10 mph, 37% SD			430000	550000	730000	1100000	1500000	1900000	2300000	2800000	3600000	4500000	5200000
	AT401, C, 10 mph, 25% SD			470000	670000	950000	1400000	2000000	2600000	3200000	3900000	5500000	7200000	8500000
	WASP, C, 10 mph, 25% SD			550000	780000	1100000	1800000	2500000	3400000	4100000	5200000	7200000	9400000	10000000
	AT401, VC, 10 mph, 20% SD			540000	820000	1300000	2100000	3000000	4100000	5200000	6700000	9400000	12000000	16000000
	WASP, VC, 10 mph, 20% SD			680000	1100000	1600000	2600000	3800000	4900000	6700000	7800000	12000000	13000000	16000000
Groundboom	<i>High Boom Very fine to Fine</i>			500000	1000000	1700000	2700000	3800000	4700000	5500000	6700000	8500000	12000000	13000000
	Low Boom Very fine to Fine			1100000	2900000	4700000	7200000	9400000	12000000	13000000	16000000	19000000	23000000	31000000
	High Boom Fine to Medium/Coarse			1900000	4900000	7200000	10000000	13000000	16000000	19000000	19000000	23000000	31000000	31000000
	Low Boom Fine to Medium/Coarse			2800000	7800000	12000000	16000000	19000000	23000000	31000000	31000000	47000000	47000000	47000000
Field Corn														
Groundboom	<i>High Boom Very fine to Fine</i>	0.05	0.0055575	700000	1400000	2300000	3800000	5300000	6600000	7700000	9400000	12000000	16000000	19000000

	Low Boom Very fine to Fine			1500000	4100000	6600000	10000000	13000000	16000000	19000000	22000000	26000000	33000000	44000000
	High Boom Fine to Medium/Coarse			2700000	6900000	10000000	15000000	19000000	22000000	26000000	26000000	33000000	44000000	44000000
	Low Boom Fine to Medium/Coarse			4000000	11000000	16000000	22000000	26000000	33000000	44000000	44000000	66000000	66000000	66000000

<sup>1</sup> No aerial application to dry beans. Only field corn and soybeans

**Appendix E. Summary of US and International Tolerances and Maximum Residue Limits**

Table E.1 - Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US		Canada	Mexico <sup>1</sup>	Codex
40 CFR 180.468  Plant/Livestock: N-(2,6-difluorophenyl)-5-methyl-(1,2,4)triazolo(1,5-a)pyrimidine-2- sulfonamide)		[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonmide, N-(2,6-difluorophenyl)-5-methyl-		None
Commodity	Tolerance (ppm) /Maximum Residue Limit (mg/kg)			
	US	Canada	Mexico <sup>2</sup>	Codex
Bean, dry, seed	0.05			
Corn, field, forage	0.05			
Corn, field, grain	0.05	0.05 field corn		
Corn, field, stover	0.05			
Soybean, seed	0.05	0.05 dry soybeans		
Completed: M. Negussie; 05/09/13				

<sup>1</sup> Mexico adopts US tolerances and/or Codex MRLs for its export purposes.