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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

DATE: 07-APR-09

SUBJECT: **Sulfentrazone**; **REVISED** Section 3 Registration Request to Add New Uses on: *Brassica*, Head and Stem, Subgroup 5A; *Brassica*, Leafy Greens, Subgroup 5B; Melon, Subgroup 9A; Fruiting Vegetable, Group 8 and Okra; Pea, Succulent; Flax; Strawberry; and Tuberous and Corm Vegetable, Subgroup 1C. **Human-Health Risk Assessment.**

PC Code: 129081
Decision No.: 388050
Petition No.: 7E7308
Risk Assessment Type: Single Chemical/Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D362324
Registration Nos: 279-3220 & 279-3189
Regulatory Action: Amended Section 3
Case No.: NA
CAS No.: 122836-35-5
40 CFR: §180.498

FROM: Kelly Lowe, Environmental Scientist
Lisa Austin, Ph.D., Toxicologist
Robert Mitkus, PhD, Toxicologist
William D. Wassell, Chemist
Risk Assessment Branch (RAB1)
Health Effects Division (HED; 7509P)

THROUGH: Dana M. Vogel, Branch Chief
George F. Kramer, Ph.D., Senior Chemist
RAB1/HED (7509P)

TO: Daniel Rosenblatt, Risk Manager 05
Registration Division (RD; 7505P)

NOTE: This document supersedes Memo, L. Austin, *et al.*, 10/7/2008 (DP# 349558). This assessment has been updated to include revisions to the toxicological endpoints.

The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that HED evaluate 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 proposed and registered uses of the herbicide sulfentrazone [*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide].

A summary of the findings are provided in this document. The original risk assessment and hazard assessment were provided by Lisa Austin (RAB1), the updated hazard assessment was

provided by Robert Mitkus (RAB1), the residue chemistry review and dietary exposure assessment were provided by William Wassell (RAB1); the occupational/residential exposure assessment and updated risk assessment were provided by Kelly Lowe (RAB1); and the drinking water assessment was provided by Michael Barrett of the Environmental Fate and Effects Division (EFED).

NOTE: In 2003, HED completed a Section 3 risk assessment for the application of sulfentrazone to caneberry (crop subgroup group 13A); wild raspberry; edible-podded legume vegetable (crop subgroup 6A); succulent shelled pea and bean (crop subgroup 6B); soybean, succulent shelled; and various tropical fruits (D274568, G. Kramer *et al.*, 28-May-2003). The current document contains only those aspects of the risk assessment which are affected by the addition of the proposed sulfentrazone uses.

TABLE OF CONTENTS

1.0 Executive Summary

Sulfentrazone is an aryl triazolinone herbicide used to control a variety of broadleaf weeds. The mode-of-action for controlling emerging weeds is by protoporphyrinogen oxidase inhibition. Sulfentrazone acts by the same mechanism as the diphenyl ether herbicides in which membrane disruption is initiated by the inhibition of protoporphyrinogen oxidase (PPO) in the chlorophyll biosynthetic pathway and leads to the subsequent build-up of toxic intermediates. Plants emerging from soils treated with sulfentrazone turn necrotic and die shortly after exposure to light. (Source: http://courses.cropsci.ncsu.edu/cs414/CH_11.PDF).

The Interregional Research Project No. 4 (IR-4) has submitted a petition proposing the establishment of permanent tolerances for the combined residues of the herbicide sulfentrazone [*N*-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1*H*-1,2,4-triazol-1-yl]phenyl]methanesulfonamide] and its metabolites HMS [*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1*H*-1,2,4-triazol-yl)phenyl)methanesulfonamide)] and DMS [(*N*-2,4- dichloro-5-[4-(difluoromethyl)-4,5-dihydro-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide] in/on:

Brassica, head and stem, subgroup 5A*	0.20 ppm
Brassica, leafy greens, subgroup 5B	0.35 ppm
Melon, subgroup 9A	0.10 ppm
Vegetable, fruiting, group 8	0.05 ppm
Okra	0.05 ppm
Pea, succulent	0.05 ppm
Flax	0.05 ppm
Strawberry	0.05 ppm
Vegetable, tuberous and corm, subgroup 1C*	0.15 ppm

*Individual tolerances are established for residues in/on cabbage at 0.20 ppm and potato at 0.15 ppm.

A tolerance is currently established under 40 CFR §180.498(a)(1) for the combined residues of sulfentrazone and its major metabolite, HMS [*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide] in/on soybean seed at 0.05 ppm. In addition, permanent tolerances are established under 40 CFR §180.498(a)(2) for the combined residues of sulfentrazone and its metabolites HMS and DMS [*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide] in/on several food commodities; these established tolerances range from 0.15 ppm (various plant commodities) to 0.40 ppm (peanut meal). Time-limited tolerances for the combined residues of sulfentrazone and its metabolites HMS and DMS have been established under 40 CFR §180.498(b) in connection with Section 18 Emergency Exemptions; these include tolerances for residues in/on bean, succulent-seed without pod (lima bean & cowpea) at 0.1 ppm with a 12/31/07 expiration date, flax seed at 0.2 ppm with a 12/31/10 expiration date, and strawberry at 0.60 ppm with a 12/31/10 expiration date. Finally, tolerances are established under 40 CFR §180.498(d) for inadvertent and indirect combined residues of sulfentrazone and its metabolites HMS and DMS in/on cereal grain (excluding sweet corn) bran, forage, grain, hay, hulls, stover, and straw at 0.1-0.6 ppm as a result of the application of sulfentrazone to growing crops.

The sulfentrazone end-use products (EPs) relevant for this registration request are Spartan® Herbicide (EPA Reg. No. 279-3189; 75% dry-flowable or DF formulation) and Spartan® 4F

Herbicide (EPA Reg. No. 279-3220; 4 lb/gal flowable-concentrate (FlC) formulation). IR-4 requests the amendment of these EP labels to incorporate new uses on head and stem *Brassica*, leafy greens *Brassica*, fruiting vegetables including okra, melons, strawberry, succulent peas and beans, and flax. These EPs are proposed for: (i) preplant or preemergence applications on all of the above-listed crops at maximum seasonal rates of 0.1875-0.375 lb ai/A using ground or aerial equipment; and (ii) postemergence applications on fruiting vegetables at a maximum seasonal rate of 0.375 lb ai/A. No pre-harvest intervals (PHIs) were proposed for these crops.

Hazard Assessment

Sulfentrazone has low acute toxicity via the oral, dermal and inhalation routes (Toxicity Category III). It is a mild eye irritant (Toxicity Category III), but not a dermal irritant or sensitizer. No dermal toxicity was seen at the limit dose (1000 mg/kg/day) in rats. Subchronic and chronic toxicity studies in rats, mice and dogs identified the hematopoietic system as the target of sulfentrazone. Protoporphyrinogen oxidase inhibition in the mammalian species may result in disruption of heme synthesis. In these studies, disturbed heme synthesis was seen at about the same dose levels across species, except in the case of mice, where the effects were seen at a slightly higher dose. These effects occurred around the same dose level from the short- through long-term exposure without increasing in severity.

Carcinogenicity studies in rats and mice showed no evidence of increased incidence of tumor formation due to treatment with sulfentrazone. Therefore, the HED Reference Dose (RfD)/Peer Review Committee classified sulfentrazone as "not likely to be carcinogenic to humans." The available mutagenicity studies indicate that sulfentrazone is weakly clastogenic in the *in vitro* mouse lymphoma assay in the absence of S9 activation; however, the response was not evident in the presence of S9 activation. Sulfentrazone is neither mutagenic *in vitro* nor clastogenic in male nor female mice *in vivo*.

Increased quantitative susceptibility in fetuses was observed in the dermal developmental study in rats. Increased qualitative susceptibility was seen in the developmental study in rabbits and the 2-generation reproduction study in rats. Evidence of developmental neurotoxicity (DNT) was observed in a DNT study published in the open literature (de Castro, *et al.*, 2007) and reviewed by HED since the last risk assessment.

Sulfentrazone is readily absorbed from the gastrointestinal (GI) tract of rats following oral dosing and nearly all radioactivity was recovered in the urine (84 - 104% of the dose) and feces (~ 6%) within 72 hours. There were no major sex-related differences in the pattern of excretion and no evidence of bioaccumulation.

Dose Response Assessment

The potential for increased susceptibility of infants and children from exposure to sulfentrazone was re-evaluated as required under the Food Quality Protection Act (FQPA) of 1996. Based on evidence of DNT that was observed in a DNT study in rats published in the open literature (de Castro, *et al.*, 2007), the FQPA safety factor was retained at 10X for several exposure scenarios for which the results of this study applied.

The acute reference dose (aRfD) for females 13-49 and the chronic reference dose (cRfD) were calculated by dividing the lowest-observed-adverse-effects-level (LOAEL) by 1000 (10X for interspecies extrapolation, 10X for intraspecies variation, and 10x for use of a LOAEL). Since

the FQPA SF has been retained for these exposure scenarios at 10X in the form of a UF_L, the acute and chronic population adjusted doses (aPAD and cPAD) are equal to the acute and chronic RfDs. The aRfD for the general population was calculated by dividing the no-observed-adverse-effects-level (NOAEL) by 100 (10X for interspecies extrapolation and 10X for intraspecies variation). Endpoints selected for dermal risk assessment for all durations were based on a single dermal developmental study. Since an oral study was selected for all durations of inhalation exposure, a 100% inhalation absorption factor was used in the route-to-route extrapolation. The level of concern for dermal exposures is for margins of exposure (MOEs) that are less than 100. The level of concern for inhalation exposures is for MOEs that are less than 1000. The following points of departure were used in this risk assessment:

Acute dietary (female 13-50 years)	LOAEL= 25 mg/kg/day	aRfD and aPAD = 0.025 mg/kg/day
Acute dietary (general population)	NOAEL = 250 mg/kg/day	aRfD and aPAD = 2.5 mg/kg/day
Chronic dietary	LOAEL = 25 mg/kg/day	cRfD and cPAD = 0.025 mg/kg/day
Short- and Intermediate-term incidental oral	NOAEL = 14 mg/kg/day	Target MOE = 100
Short-, Intermediate-, and Long-term dermal	Dermal NOAEL = 100 mg/kg/day	Target MOE = 100
Short-, Intermediate-, and Long-term inhalation	Oral LOAEL = 25 mg/kg/day	Target MOE = 1000

Note that while the new 40 CFR revised Part 158 requirement for an immunotoxicity study has not yet been fulfilled, the existing data are sufficient for endpoint selection for exposure/risk assessment scenarios and for evaluation of the requirements under FQPA. Further, the data requirements pertaining to immunotoxicity (see Section 9.1) should be fulfilled as a condition of registration.

Exposure Assessment

Dietary Exposure and Risk

The acute and chronic dietary exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model - Food Consumption Intake Database (DEEM-FCID™, ver. 2.03). DEEM-FCID™ incorporates food consumption data from the United States Department of Agriculture (USDA) Continuing Surveys of Food Intakes by Individuals (CSFII; 1994-1996 and 1998). The current assessment is being conducted in support of new uses on *Brassica*, head and stem, subgroup 5a; *Brassica*, leafy greens, subgroup 5b; melon, subgroup 9a; fruiting vegetable, group 8 and okra; pea, succulent; flax; strawberry; and tuberous and corm vegetable, subgroup 1c.

The acute analysis assumed DEEM™ (ver. 7.81) default processing factors, 100% crop-treated (CT) and tolerance-level residues for all commodities. The acute analysis also incorporated the drinking water estimates provided by EFED. The estimated drinking water concentrations (EDWCs) were Tier 1 estimates for groundwater using the SCI-GROW model (Screening Concentration In GROund Water) and surface water using the FQPA Index Reservoir Screening Tool (First) model) for sulfentrazone and 3-carboxylic acid sulfentrazone. The models utilized an application rate of 0.375 lbs ai/A with 2 applications per season. EDWCs of 0.0358 ppm and 0.026 ppm were used in the acute and chronic analysis, respectively. The resulting acute food

plus water exposure estimates are not of concern to HED (<100% aPAD) at the 95th percentile of the exposure distribution for the U.S. general population (<1% aPAD), and all population subgroups; the most highly exposed population subgroup was all infants (<1 year old) with <1% aPAD. As the aPAD is different for females 13 to 49 years old, the resulting acute exposure estimate for females 13 to 49 years old was 13% of the aPAD.

The chronic analysis assumed DEEM™ (ver. 7.81) default processing factors, 100% CT and tolerance-level residues for all commodities. The chronic analysis also incorporated the drinking water estimates provided by EFED (see above). The resulting chronic exposure estimates are not of concern to HED. The most highly exposed population was children 1-2 years old utilizing 14% of the cPAD.

Aggregate Risk

Acute and chronic aggregate risks are made up only of dietary sources; therefore, the exposure estimates provided in the dietary exposure analysis represent acute and chronic aggregate exposure, respectively. Short- and intermediate-term aggregate risks are made up of dietary and non-dietary sources of exposure. Since sulfentrazone is proposed for use on turf (application by professional applicators only), post-application residential exposure is expected. Only short-term aggregate risk was estimated since the use pattern is not expected to result in exposure of more than a 30-day duration. Short-term aggregate risk is made up of average dietary exposures from food and drinking water sources plus dermal and oral (children only) residential exposures. Dietary (food and drinking water) exposure is based on a Tier 1 chronic dietary exposure assessment. An aggregate cancer risk assessment was not performed because sulfentrazone is not considered to be a carcinogen. The aggregate short-term MOEs are ≥100; therefore, aggregate exposures to sulfentrazone are not of concern to HED.

Residential Exposure Estimates

There are no proposed residential uses at this time; however, there is an existing residential turf use. Sulfentrazone is registered for use on residential lawns and turf, as well golf courses (D289349, M. Dow, 15-May-2003). Sulfentrazone can be applied by professional lawn-care operators to residential lawns and to golf courses. No homeowner handler exposure is anticipated from normal application of sulfentrazone. Post-application exposure was estimated for toddler hand-to-mouth activity, toddler object-to-mouth activity, toddler dermal contact and adult dermal contact to treated residential turf. All residential exposure and risk estimates are below HED's level of concern (MOEs ≥100). A post-application exposure assessment was conducted for adult and adolescent golfers. Exposure and risk estimates for golfers are below HED's level of concern (MOEs ≥100).

Occupational Exposure Estimates

Sulfentrazone is proposed as a soil-applied herbicide for the control of susceptible broadleaf, grass and sedge weeds on head and stem *Brassica*, leafy green *Brassica*, melons, fruiting vegetables, okra, succulent peas, flax, strawberry, and tuberous and corm vegetables, and also impregnation to dry bulk fertilizer and application with dry fertilizer. Soil applications of sulfentrazone must be made before crop germination to prevent injury to the emerging crop seedlings. Sulfentrazone may be applied to the soil at early preplant, preplant incorporated, or preemergence using aerial, chemigation, and groundboom application equipment. Sulfentrazone also may be applied as a hooded postemergence spray between the rows of fruiting vegetables and okra using shielded groundboom equipment.

The estimated risks for workers based on the short- and intermediate-term dermal and inhalation exposures at baseline do not exceed HED's level of concern (i.e., MOEs ≥100 for dermal and ≥1000 for inhalation), provided workers wear protective gloves as recommended on the label. It should be noted that only engineering control data are available to assess dermal and inhalation risks to handlers operating aircraft (enclosed cockpit) and to commercial handlers participating in dry bulk fertilizer impregnation (closed mixing/loading/application systems). The risks are not a concern for pilots using enclosed cockpits and for commercial handlers involved in dry bulk fertilizer impregnation using closed mixing/loading/application systems and wearing baseline attire. The only current engineering control data for closed mixing/loading of water-dispersible granules is water-soluble packaging, however, these data are only used as a surrogate since no other data are available. The use of this data does not require that the sulfentrazone product be re-formulated.

Post-application risks were assessed and were found to not exceed HED's level of concern on Day 0 (12 hours following application). Therefore, the restricted-entry interval (REI) is based on the acute toxicity of sulfentrazone technical material which is classified as Category III for acute dermal toxicity and for eye irritation potential and Category IV for skin irritation potential. Sulfentrazone is not a dermal sensitizer. Under the Worker Protection Standard (WPS) for Agricultural Pesticides, active ingredients classified as acute toxicity categories III or IV for these routes are assigned a 12-hour REI. Therefore, the 12-hour REI that appears on the proposed label is adequate.

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), were previously determined to require a review of their ethical conduct, and have received that review. The studies in PHED were considered appropriate (or ethically conducted) for use in risk assessments.

Environmental Justice Considerations
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.hss.energy.gov/nuclearsafety/env/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 USDA under CSFII 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, season of the year, ethnic group, and region of the country. 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.

Regulatory Recommendations
Provided a revised Section B (proposed use directions), a revised Section F (proposed tolerances), and a reference standard for the metabolite HMS are submitted, the residue chemistry, toxicology and occupational exposure databases support conditional registration and establishment of permanent tolerances. The proposed uses and the submitted data support the establishment of tolerances for the combined residues of free and conjugated sulfentrazone and its metabolites HMS and DMS in/on:

Brassica, head and stem, subgroup 5A	0.20 ppm
Brassica, leafy greens, subgroup 5B	0.40 ppm
Melon, subgroup 9A	0.15 ppm
Vegetable, fruiting, group 8	0.15 ppm
Okra	0.15 ppm
Pea, succulent	0.15 ppm
Flax	0.15 ppm
Strawberry	0.15 ppm
Vegetable, tuberous and corm, subgroup 1C	0.15 ppm

Unconditional registration can be granted following submission of adequate flax and tomato processing studies and an immunotoxicity study.

Note to RD and registrant: As the enforcement method for plant commodities determines free and conjugated forms of the analytes, the tolerance expression should be revised to indicate tolerances are established for **combined residues of free and conjugated forms of sulfentrazone, and its metabolites HMS and DMS**. Tolerances should be proposed using this tolerance expression. As the proposed directions for use on fruiting vegetables include postemergence applications, HED concludes metabolism data are not available to support the postemergence applications.

2.0 Ingredient Profile

Sulfentrazone is an aryl triazolinone herbicide used to control a variety of broadleaf weeds. The mode-of-action for controlling emerging weeds is by PPO inhibition. Sulfentrazone acts by the same mechanism as the diphenyl ether herbicides in which membrane disruption is initiated by the inhibition of PPO in the chlorophyll biosynthetic pathway and leads to the subsequent build-up of toxic intermediates. Plants emerging from soils treated with sulfentrazone turn necrotic and die shortly after exposure to light.

2.1 Summary of Proposed Uses

A list of the sulfentrazone end-use products relevant to this registration request is presented in Table 2.1.a. The proposed crop use directions are summarized in Table 2.1.b. Information regarding rotational crop restrictions is listed in Table 2.1.c.

Table 2.1.a. Summary of Proposed End-Use Products.

Trade Name	Reg. No.	ai (% of formulation)	Formulation Type[1]	Target Crops	Target Pests	Label Date
Spartan® 4F Herbicide	279-3220	39.6 (4 lb/gal)	FlC	Row Crops: corn (field, seed, and pop); peanut; potato; soybean; sugarcane; sunflower; tobacco. Vegetable Crops: asparagus; *Brassica*, head and stem; *Brassica*, leafy greens; cabbage (transplant only); dry shelled beans and peas; fruiting vegetables (except cucurbits) and okra; horseradish; melons; strawberry; succulent peas and beans; Oil Crops: flax; mint.	Broadleaf, grass, and sedge weeds.	Specimen label code: Spartan4F _3_12-17-07
Spartan® Herbicide	279-3189	75	DF			Specimen label code: Spartan _3_12-17-07

[1] FlC = flowable-concentrate formulation; DF = dry-flowable formulation.

Table 2.1.b. Summary of Proposed Directions for Use of Sulfentrazone.

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate, lb ai/A [Soil Type]	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)
Brassica, Head and Stem [broccoli, Chinese broccoli, Brussels sprouts, Chinese (napa) cabbage, Chinese mustard, cauliflower, cavalo broccoli, kohlrabi]					
Early preplant, preemergence, preplant incorporated	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.281 [coarse] 0.094-0.375 [medium and fine]	Not specified (NS)	0.375	NS
	Use Directions and Limitations: Do not incorporate to depths greater than 2 inches.				
Brassica, Leafy Greens [broccoli raab, Chinese (bok choy) cabbage, collards, kale, mizuna, mustard greens, mustard spinach, rape greens]					
Early preplant, preemergence, preplant incorporated	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.281 [coarse] 0.094-0.375 [medium and fine]	NS	0.375	NS
	Use Directions and Limitations: Do not incorporate to depths greater than 2 inches.				
Fruiting Vegetables (except curcurbits) [eggplant, groundcherry *(Physalis* spp), pepino, pepper (includes bell pepper, chili pepper, cooking pepper, pimento, sweet pepper), tomatillo, tomato] and okra					
Preplant banded or postemergence with shielded/hooded sprayer	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.281 [coarse] 0.094-0.375 [medium and fine]	NS	0.375	NS
	Use Directions and Limitations: None.				

Table 2.1.b. Summary of Proposed Directions for Use of Sulfentrazone.

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate, lb ai/A [Soil Type]	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)
Succulent Peas and Beans [bean (Phaseolus; includes green lima bean and succulent broad bean), bean (*Vigna*; includes blackeyed pea, cowpea, southern pea), pea (*Pisum*; includes English pea, garden pea, green pea); pigeon pea					
Preemergence	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.1875 [coarse] 0.094-0.1875 [medium] 0.117-0.1875 [fine]	NS	0.1875	NS
	Use Directions and Limitations: Do not incorporate.				
Flax					
Preemergence	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.281 [coarse] 0.094-0.375 [medium and fine]	NS	0.375	NS
	Use Directions and Limitations: Do not apply directly on crop after the crop emergence or if the seedling sprouts are close to the soil surface.				
Melon [citron melon, muskmelon, watermelon]					
Preemergence	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.093-0.1875 [coarse] 0.093-0.2125 [medium] 0.117-0.25 [fine]	NS	0.25	NS
	Use Directions and Limitations: Do not apply directly on crop after the crop emergence or if the seedling sprouts are close to the soil surface.				
Strawberry					
Preemergence	4 lb/gal FlC [279-3220] 75% DF [279-3189]	0.070-0.281 [coarse] 0.094-0.375 [medium and fine]	NS	0.375	NS
	Use Directions and Limitations: Do not apply directly on crop after the crop emergence or if the seedling sprouts are close to the soil surface.				

The following restrictions apply to all proposed crops: *Application rates are dependent on soil texture, percent organic matter (%OM), and pH. Use on soils classified as sand which have <1% OM is prohibited. Applications are to be made in a minimum of 10 gallons per acre (GPA) using ground equipment or a minimum of 5 GPA using aerial equipment.*

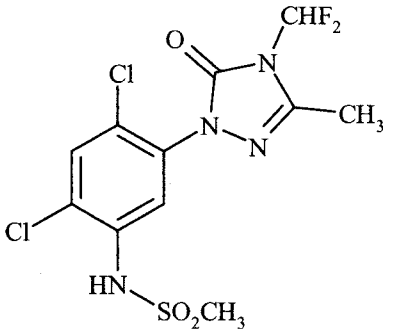
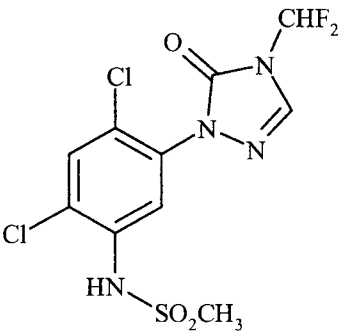
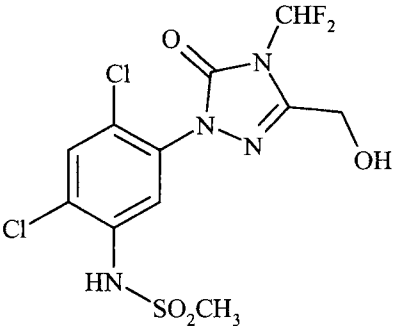
Table 2.1.c. Plantback Intervals for Use of Sulfentrazone.	
Rotational Crop[1]	Plantback Interval (months)
Alfalfa	12
Barley	4
Cabbage	Anytime
Canola	24
Cereal Grains (Buckwheat, Oats, Pearl Millet, Proso Millet, Teosinte, Wild Rice)	12
Corn, Field	10
Corn, Pop	18
Corn, Sweet	18
Cotton	18
Dry Shell Peas and Beans	Anytime
Horseradish	Anytime
Limas	Anytime
Mint	Anytime
Peanuts	Anytime
Potatoes	Anytime
Rice	10
Rye	4
Sorghum	10 [2]
Soybean	Anytime
Sugar Beets	36
Sugarcane	Anytime
Sunflowers	Anytime
Sweet Potatoes	12
Triticale	4
Tobacco	Anytime
Turf	Anytime
Wheat	4

[1] For all other crops not listed, the rotation interval is a minimum of 12 months.
[2] Sorghum – 18-month rotation for rates above 8.0 oz/A.

Conclusions. The use directions are adequate to allow HED to conduct an assessment of whether the submitted residue data reflect the maximum residues likely to occur. However, the label for Spartan® 4F Herbicide (EPA Reg. No. 279-3220), a 4 lb/gal FlC (liquid) formulation, should be modified to correct the application rates listed as "dry ounces Spartan® Herbicide per acre" to "fluid ounces Spartan® Herbicide per acre." Also, as metabolism data are not available to support postemergence applications on fruiting vegetables (except curcurbits), these proposed uses should be limited to preemergence application only. Additionally, the proposed labels should be revised to specify a maximum single and seasonal application rate of 0.020 lb ai/A to *Brassica* leafy greens, subgroup 5B, as this rate is supported by the submitted crop field trial data for mustard greens. A revised Section B is required.

2.2 Structure and Nomenclature

Table 2.2. Structure and Nomenclature of Sulfentrazone and Its Metabolites.

Chemical structure	
Common name	Sulfentrazone
Company experimental name	F6285; FMC 97285
IUPAC name	2',4'-dichloro-5'-(4-difluoromethyl-4,5-dihydro-3-methyl-5-oxo-1*H*-1,2,4-triazol-1-yl)methanesulfonanilide
CAS name	*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide
CAS registry number	122836-35-5
End-use product (EP)	4 lb/gal FlC formulation (Spartan® 4F Herbicide; EPA Reg. No. 279-3220) and 75% DF formulation (Spartan® Herbicide; EPA Reg. No. 279-3189)
Chemical structure of DMS metabolite	
Common name	3-desmethyl sulfentrazone; DMS
Chemical name	*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide
Chemical structure of HMS metabolite	
Common name	3-hydroxymethyl sulfentrazone; HMS
Chemical name	*N*-(2,4-dichloro-5-(4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl)methanesulfonamide

2.3 Physical and Chemical Properties

Table 2.3 Physicochemical Properties of Technical Grade Sulfentrazone.		
Parameter	Value	Reference
Melting range	120-122 °C	DP# 288712, 3/6/03, G. Kramer, G. Reddy, and L. Liu
pH	4.78 at 23 °C	
Density	0.53 g/cm^3	
Water solubility	4.0 x 10^2 µg/g	
Solvent solubility	18.6% w/w in acetonitrile	
Vapor pressure	8 x 10^{-10} mm Hg	
Dissociation constant, pK_a	6.56	
Octanol/water partition coefficient, Log(K_{OW})	1.49 at pH 5	
UV/visible absorption spectrum	Not available	

3.0 Hazard Characterization/Assessment

A detailed hazard characterization and dose response assessment for sulfentrazone were presented in a previous HED risk assessment (D274568, G. Kramer *et al.*, 28-May-2003). However, both the hazard characterization and toxicity profile tables have been updated since the last risk assessment based on additional data reviewed by the Agency.

Sulfentrazone has low acute toxicity via the oral, dermal and inhalation routes (Toxicity Category III). It is a mild eye irritant (Toxicity Category III), but not a dermal irritant or sensitizer. No dermal toxicity was seen at the limit dose (1000 mg/kg/day) in a 28-day dermal toxicity study in rats. Subchronic and chronic toxicity studies in rats, mice and dogs identified the hematopoietic system as the target of sulfentrazone. Protoporphyrinogen oxidase inhibition in the mammalian species may result in disruption of heme synthesis. In these studies, disturbed heme synthesis was seen at about the same dose levels (LOAELs of 57 to 83 mg/kg/day) across species, except in the case of mice, where the effects were seen at a slightly higher dose (LOAELs of 94 - 108 mg/kg/day). These effects occurred around the same dose level from the short- through long-term exposure without increasing in severity. Sulfentrazone is readily absorbed from the GI tract of rats following oral dosing and nearly all radioactivity was recovered in the urine (84 - 104% of the dose) and feces (~ 6%) within 72 hours. There were no major sex-related differences in the pattern of excretion and no evidence of bioaccumulation.

Carcinogenicity studies in rats and mice showed no evidence of increased incidence of tumor formation due to treatment with sulfentrazone. The HED RfD/Peer Review Committee, which met on February 15, 1996 and April 4, 1996, classified sulfentrazone as "not likely to be carcinogenic to humans" in accordance with the EPA proposed Guidelines for Carcinogenic Risk Assessment (April 10, 1996). The available mutagenicity studies indicate that sulfentrazone is weakly clastogenic in the *in vitro* mouse lymphoma assay in the absence of S9 activation; however, the response was not evident in the presence of S9 activation. Sulfentrazone is neither mutagenic in bacterial cells nor clastogenic in male nor female mice *in vivo*.

Developmental effects such as decreased fetal body weights and increased skeletal variations in the dermal study occurred at doses that were not maternally toxic, indicating increased quantitative susceptibility. In rabbits, developmental effects such as decreased pup viability were observed at a maternally-toxic dose (clinical signs, abortions and decreased body-weight gains), indicating increased qualitative susceptibility due to the severity of the developmental effects. In

the 2-generation reproduction study in rats, offspring effects such as decreased litter survival (more severe than maternal effects) were observed at the slightly maternally-toxic dose (slightly decreased body-weight gain), indicating increased qualitative susceptibility.

In the acute neurotoxicity study an increased incidence of clinical signs (staggered gait, splayed hind limbs, and abdominal gripping) and decreased functional-observation battery (FOB) parameters and motor activity were observed at 750 and 2000 mg/kg/day; however, these findings were of short duration. Complete recovery was observed in 14 days and there was no evidence of neuropathology. In the subchronic neurotoxicity study, systemic toxicity was seen at 2500 (M/F; 150/180 mg/kg/day) and 5000 (M/F; 265/292 mg/kg/day) ppm; however, there was no evidence of neuropathology due to treatment. In a published DNT study in the rat (de Castro, *et al.*, 2007 [1]), a statistically significant, dose-dependent delay in ear opening was observed in pups whose mothers were treated with ≥25 mg/kg/day sulfentrazone on gestation day (GD) 1-6 or GD 6-15 (note: postnatal exposure of pups did not take place as in a guideline DNT study). A dose-dependent decrease in grip response (25%) and a 3-fold increase in reaction time for the surface righting reflex were observed on day 2 of age in pups whose mothers were treated with sulfentrazone on GD 6-15. Righting reflex reaction time returned to control levels in pups by day 5 of age, whereas grip response did not. Rearing frequency in the open field was also dose-dependently decreased on days 30, 60, and 90 of age in offspring whose mothers were treated on GD 1-6. Using the method of Cumming, *et al.*, (2007 [2]), HED concluded that each of these effects was statistically significant at ≥25 mg/kg/day. Therefore, the observed changes in behavioral parameters in pups at the 25 mg/kg/day dose level; the increase in severity or incidence for each of these parameters at the next dose level (50 mg/kg/day); the increase in number of parameters affected (including body weight) at the next dose level (50 mg/kg/day); and the statistical significance of the effects point to a biologically significant effect on the development of motor function in pups whose mothers were exposed to sulfentrazone during gestation.

3.1 Updated Toxicity Endpoint Selection and FQPA Considerations

The doses and toxicological endpoints selected for several exposure scenarios have been updated since the last risk assessment based on a DNT study (de Castro, *et al.*, 2007) published recently in the academic literature and reviewed by HED. The rationale for the changes is provided below and the updated endpoints are included in Table 3.1.

Acute Dietary Endpoint (Females 13 - 49 yrs old): A published DNT study in the rat (de Castro, *et al.*, 2007) was used to select the dose and endpoint for establishing the aRfD for females aged 13-49 years old. In this study, several statistically significant and dose-dependent effects were observed in pups whose mothers were treated with ≥ 25 mg/kg/day sulfentrazone on GD 1-6 or GD 6-15 (note: postnatal exposure of pups did not take place as in a guideline DNT study). Although dams were treated repeatedly in this study and it is unclear whether the effects occurred following one or more than one dose in the study, it has been HED's practice to consider various forms of developmental toxicity as single-dose effects and, therefore, relevant for the acute dietary (females aged 13-49) exposure scenario, in order to protect against potential exposure of pregnant females. Because developmental toxicity was observed at the lowest dose tested in this study, there is no NOAEL. Therefore, the FQPA safety factor is 10X for the use of a LOAEL as the point of departure in the absence of a NOAEL for this exposure scenario. This

1 de Castro VL, Destefani CR, Diniz C, Poli P. 2007. Evaluation of neurodevelopmental effects on rats exposed prenatally to sulfentrazone. Neurotoxicology 28(6):1249-59.

2 Cumming G, Fidler F, Vaux DL. 2007. Error bars in experimental biology. J Cell Biol 177(1):7-11.

decision is supported by the lack of an effect on maternal body weight during gestation at any dose tested, although this was the only parameter tested during gestation in dams.

Acute Dietary Endpoint (General population, including infants and children): The current endpoint remains valid for this exposure scenario, since the published DNT study is relevant only to pregnant females.

Chronic Dietary Endpoint (All populations): The published DNT study in the rat (de Castro, *et al.*, 2007) was used to select the dose and endpoint for establishing the cRfD. In this study, statistically significant, dose-dependent effects were observed in offspring at ≥25 mg/kg/day in pups whose mothers were treated with sulfentrazone on GD 1-6 or GD 6-15. Because dams were treated repeatedly in this study, it is unclear whether the effects occurred following one or more than one dose in the study. Choice of this study protects against potential chronic exposure of women during their lifespan, which would include their childbearing years. Because developmental toxicity was observed at the lowest dose tested in this study, there is no NOAEL. Therefore, the FQPA safety factor is 10X for this exposure scenario for the use of a LOAEL as the point of departure in the absence of a NOAEL. As a result, the extrapolated NOAEL for this study is 2.5 mg/kg/day, which is lower and more protective than the previously used NOAEL of 14 mg/kg/day observed in the 2-generation reproduction study.

Incidental oral endpoint: The current endpoint remains valid for the incidental oral exposure scenarios, since the published DNT study is relevant only to pregnant females.

Dermal endpoints: The current endpoint, based on developmental toxicity observed in a dermal developmental toxicity study in rats, remains valid for the dermal exposure scenarios for the following reasons: 1) the study is a route-specific study; and 2) the NOAEL for the study is lower than the dermal equivalent dose calculated for the LOAEL of the published DNT study. The dermal equivalent dose for the DNT study was calculated using the dermal absorption value of 10% that was estimated for sulfentrazone by the HIARC in 2003 (dermal equivalent dose = 25 mg/kg/day ÷ 10% = 250 mg/kg/day).

Inhalation endpoints: The published oral DNT study in the rat (de Castro, *et al.*, 2007) was used to select the dose and endpoint for the inhalation exposure scenarios. Choice of this study protects against potential subchronic and chronic exposure of women during their lifespan, which would include their childbearing years, via the inhalation route. Because developmental toxicity was observed at the lowest dose tested in this study, there is no NOAEL. Therefore, the FQPA safety factor is 10X for this exposure scenario for the use of a LOAEL in the absence of a NOAEL. As a result, the extrapolated NOAEL for this study is 2.5 mg/kg/day, which is lower and more protective than the previously used NOAEL of 14 mg/kg/day observed in the 2-generation reproduction study. In the absence of inhalation absorption data, 100% inhalation absorption is assumed.

There was no evidence of adverse effects on the organs of the immune system at the LOAEL in the sulfentrazone database. In addition, sulfentrazone does not belong to a class of chemicals (e.g., the organotins, heavy metals, or halogenated aromatic hydrocarbons) that would be expected to be immunotoxic. Based on the above considerations, HED does not believe that conducting a special series 870.7800 immunotoxicity study will result in a point of departure less than the cRfD extrapolated NOAEL of 2.5 mg/kg/day for sulfentrazone; therefore, an additional uncertainty factor (UF_{DB}) for database uncertainties does not need to be applied. It is noted that

the FQPA SF is 10X for those exposure scenarios that utilize a LOAEL as the point of departure in the absence of a NOAEL.

Table 3.1. Summary of Toxicological Doses and Endpoints for Sulfentrazone for Use in Human-Health RiskAssessments.

Exposure Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-49)	LOAEL = 25 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X (includes UF_L)	**aRfD** = aPAD = 0.025 mg/kg/day	Developmental Neurotoxicity Study (de Castro, *et al.*, 2007 [1]) - Rat LOAEL = 25 mg/kg/day, based on dose-dependent, statistically significant delayed ear opening, decreased grip response and rearing frequency, and increased surface righting reflex reaction time.
Acute Dietary (General population including infants and children)	NOAEL = 250 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	**Acute RfD = 2.5 mg/kg/day** **aPAD** = 2.5 mg/kg/day	Acute-Neurotoxicity Study - Rat LOAEL = 750 mg/kg/day based on increased incidence of clinical signs and FOB parameters and decreased motor activity.
Chronic Dietary (all populations)	LOAEL= 25 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X (includes UF_L)	**cRfD** = cPAD = 0.025 mg/kg/day	Developmental Neurotoxicity Study (de Castro, *et al.*, 2007) - Rat LOAEL = 25 mg/kg/day, based on dose-dependent, statistically significant delayed ear opening, decreased grip response and rearing frequency, and increased surface righting reflex reaction time.
Short- and intermediate -Term Incidental Oral (1-30 days, 1-6 months)	Offspring NOAEL= 14 mg/kg/day	UF_A = 10X UF_H = 10X	Residential LOC for MOE = 100	2-Generation Reproduction Study LOAEL = 33 mg/kg/day based on decreased pup body weights during lactation in both generations.
Dermal Short-, intermediate -, and long-Term (1-30 days, 1-6 months, > 6 months)	NOAEL= 100 mg/kg/day	UF_A = 10X UF_H = 10X	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	Dermal Developmental Study - Rat LOAEL = 250 mg/kg/day based on decreased fetal body weight; increased incidences of fetal variations: hypoplastic or wavy ribs, incompletely ossified lumbar vertebral arches, and incompletely ossified ischia or pubes; and reduced number of thoracic vertebral and rib ossification sites.
Inhalation Short-, Intermediate -, and long-Term (1-30 days, 1-6 months, > 6 months)	LOAEL= 25 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 10X (includes UF_L) 100% inhalation absorption assumed	Residential LOC for MOE = 1000 Occupational LOC for MOE = 1000	Developmental Neurotoxicity Study (de Castro, *et al.*, 2007) - Rat LOAEL = 25 mg/kg/day, based on dose-dependent, statistically significant delayed ear opening, decreased grip response and rearing frequency, and increased surface righting reflex reaction time.

Table 3.1. Summary of Toxicological Doses and Endpoints for Sulfentrazone for Use in Human-Health RiskAssessments.

Cancer (oral, dermal, inhalation)	**Classification:** "sulfentrazone is classified as "not likely to be carcinogenic to humans."

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = extrapolation for use of a LOAEL in the absence of a NOAEL. FQPA SF = FQPA Safety Factor. PAD = population-adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure, LOC = level of concern.

3.2 Recommendation for Aggregate Exposure Risk Assessments

As per FQPA, 1996, when there are potential residential exposures to a pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. Acute and chronic aggregate risks are made up only of dietary sources. Short- and intermediate-term aggregate risks are made up of dietary and non-dietary sources of exposure. Since sulfentrazone is proposed for use on turf (application by professional applicators only), post-application residential exposure is expected. Only short-term aggregate risk was estimated since the use pattern is not expected to result in exposure of more than a 30-day duration. Short-term aggregate risk is made up of average dietary exposures from food and drinking water sources plus dermal and oral (children only) residential exposures. Dietary (food and drinking water) exposure is based on a Tier 1 chronic dietary exposure assessment. An aggregate cancer risk assessment was not performed because sulfentrazone is not considered to be a carcinogen.

3.3 Endocrine Disruption

EPA is required under the Federal Food, Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, sulfentrazone may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Dietary Exposure/Risk Characterization

The assessment of the residue chemistry data submitted in support of the proposed petition was completed on 9/29/2008 (Memo, W. Wassell, D349321). The drinking water assessment was

completed by EFED on 28-AUG-2008 (Memo, M. Barrett, DP#: 349322). The dietary exposure assessment was completed by HED on 4/3/2009 (Memo, W. Wassell, D362644).

4.1 Comparative Metabolic Profile

Nature of the Residue in Plants, Livestock, and Rotational Crops

Data concerning the metabolism of sulfentrazone in soybeans and confined rotational crops were submitted in conjunction with the petition for use on soybeans (PP#4F04407). Sulfentrazone in plant commodities is metabolized via four different pathways: (1) Oxidation of the 3-methyl group to form HMS, followed by further oxidation to form sulfentrazone carboxylic acid which is decarboxylated to DMS. (2) Hydrolysis of the trifluoromethyl group to form desdifluoromethyl sulfentrazone which is oxidized and decarboxylated to form desdifluoromethyl desmethyl sulfentrazone. (3) Hydrolysis of the sulfonamide group to form desmethylsulfonyl sulfentrazone. (4) Scission of the phenyl and triazole rings to produce methyl triazole. The corresponding phenyl metabolites are believed to remain bound.

The HED Metabolism Committee has determined that the parent compound, sulfentrazone, and the metabolite HMS are the residues of concern in soybeans, and that sulfentrazone and the metabolites HMS and DMS are the residues of concern in rotational crops (D226434, 6/14/96, G. Kramer). In addition, HED concluded that the results of the rotational crop metabolism studies may be translated to support preemergent uses on all types of crops (D220548, 3/13/96, G. Kramer).

For the proposed uses of sulfentrazone, limited to preemergence application, the nature of the residue in crops is understood. The residues of concern are sulfentrazone and its metabolites HMS and DMS. However, as the enforcement method for plant commodities determines free and conjugated forms of the analytes, the tolerance expression should be revised to indicate the residues of concern are the combined residues of free and conjugated sulfentrazone, and its metabolites HMS and DMS. Additionally, as the proposed directions for use on fruiting vegetables include postemergence applications, HED concludes metabolism data are not available to support the postemergence applications.

Adequate ruminant and poultry metabolism studies were submitted in conjunction with the soybean petition (PP#4F04407). The metabolism of sulfentrazone in livestock differs from that in plants as metabolism proceeds only by oxidation of the 3-methyl group to HMS, followed by further oxidation to form sulfentrazone carboxylic acid which is decarboxylated to DMS. Sulfentrazone *per se* and its metabolites HMS and DMS were identified as the residues of concern in meat, milk, poultry and eggs.

The residues of concern in primary crops, rotational crops, livestock, and drinking water are shown in Table 4.1 below.

Table 4.1. Residues of Concern in Crops, Livestock, and Drinking Water.

Matrix	Tolerance Expression	Residues for Risk Assessment
Primary Crops	sulfentrazone, HMS (free and conjugated)	sulfentrazone, HMS (free and conjugated)
Rotational Crops	sulfentrazone, HMS, DMS (free and conjugated)	sulfentrazone, HMS, DMS (free and conjugated)
Livestock	sulfentrazone, HMS, DMS	sulfentrazone, HMS, DMS
Water	Not applicable.	Sulfentrazone, 3-carboxylic acid sulfentrazone

4.2 Drinking Water Residue Profile

The previous drinking water exposure assessment for the multiple uses of sulfentrazone can be used in place of a new assessment for the currently proposed multiple uses of Spartan® 4F (39.6% ai) and Spartan® 75DF (75% ai). For a complete summary of the drinking water assessments for sulfentrazone see the EFED memos; R. Parker (17-APR-2003; D284975) and M. Barrett (28-AUG-2008; DP#: 349322).

EFED provided Tier 1 EDWCs for groundwater (using the SCI-GROW model) and surface water (using the FIRST model) for sulfentrazone and 3-carboxylic acid sulfentrazone (see Table 4.2 below). These values generally represent upper-bound conservative estimates of the total residue concentrations that might be found in surface water and groundwater due to the use of sulfentrazone on sugarcane, cabbage, potatoes, mint or horseradish. These crops were chosen for this assessment because the label permits use of the maximum application rate (0.375 lb ai/A) and aerial application. Aerial application has the potential for spray drift and is not compatible with soil incorporation which would reduce surface water concentration values.

Table 4.2. Estimated Tier 1 Concentrations of Sulfentrazone and 3-Carboxylic Acid Sulfentrazone in Drinking Water

Chemical	Surface Water (ppb)		Groundwater (ppb)
	Acute	Chronic	Acute and Chronic
Sulfentrazone	32.0	5.1	15.7
3-Carboxylic Acid Sulfentrazone	3.8	2.7	10.3
Total	35.8	7.8	26.0

4.3 Food Residue Profile

Residue Analytical Methods

Enforcement method

A gas chromatographic (GC) analytical method for the determination of free and conjugated residues of sulfentrazone, DMS, and HMS in/on various matrices was submitted with a petition for a sulfentrazone tolerance on soybeans (PP# 4F04407). A petition method validation was successfully completed by the Agency's Analytical Chemistry Laboratory (ACL). The limit of quantification (LOQ) and limit of detection (LOD) were determined to be 0.05 ppm and 0.005-0.025 ppm, respectively. HED concluded that the method is suitable for enforcement purposes (D233520, G. Kramer, 3/25/97). The method was forwarded to the Food and Drug Administration (FDA) for inclusion in the Pesticides Analytical Manual, volume II (PAM II, Letter, G. Kramer, 9/18/98). This method is suitable for enforcement of the tolerances associated with this petition.

Data-collection methods

Samples of raw agricultural commodities (RACS) and processed commodities were analyzed for residues of sulfentrazone and its metabolites DMS and HMS using the FMC method entitled, "Analytical Methodology for the Determination of Sulfentrazone, 3-Desmethyl Sulfentrazone, and 3-Hydroxymethyl Sulfentrazone in/on Various Matrices, Study Number 162MVL96R1" with minor modifications. Residues in/on broccoli and mustard greens were determined using GC equipped with a halogen-specific detector (XSD), while residues in/on cantaloupe, fruiting vegetables (pepper and tomato), peas, flax, and strawberry were determined using a liquid

chromatograph equipped with tandem mass spectrometers (LC/MS/MS) method. The data-collection methods described above are adequate based on acceptable method validation and concurrent recovery data.

Multiresidue Method (MRM)
MRM data for sulfentrazone and HMS were previously submitted and forwarded to FDA (Memo, 2/7/95, G. Kramer). Neither compound was recovered by any of the protocols. The FDA PESTDATA database dated 10/99 (PAM Vol. I, Appendix II) indicates that DMS is not recovered using MRM Sections 303 (Mills, Onley, and Gaither; Protocol E, nonfatty) and 304 (Mills, fatty food). No information for recovery of DMS using Section 302 (Luke Method; Protocol D) is available.

Magnitude of Residues in Plants

Vegetable, tuberous and corm, subgroup 1C
No new tuberous and corm vegetable field trial data were submitted. An individual tolerance has been established for the combined residues of sulfentrazone and its metabolites HMS and DMS in/on potato at 0.15 ppm [40 CFR §180.498(a)(2)]. Since potato is the representative commodity for the tuberous and corm vegetable, subgroup 1C, IR-4 is proposing to convert the individual tolerance for potato to a crop subgroup 1C tolerance at the same level.

The available potato field trial data (MRID 45582201) were reviewed in conjunction with PP#2E6405. Fourteen potato field trials were conducted in WA (3 trials), ID (2 trials), ME, FL, NC, OH, CO, ND, NJ, NY, and CA at seasonal application rates of 0.375 lb ai/A (1x the maximum proposed seasonal rate) with PHIs of 68-158 days. The maximum combined residues of sulfentrazone and its metabolites HMS and DMS were 0.077 ppm in/on treated potato tubers.

Conclusions. The previously submitted residue data for potato are adequate to support the proposed crop subgroup tolerance of 0.15 ppm for residues in/on tuberous and corm vegetables, subgroup 1C.

Brassica, head and stem, subgroup 5A

Broccoli (47311401.der.doc)

Residues of sulfentrazone, DMS, and HMS were each below the LOQ (<0.05 ppm) in/on all samples of broccoli harvested 45-73 days following one broadcast application either to soil 72 hours prior to transplanting or to direct seeded broccoli at the 2- to 4-leaf growth stage at a rate of 0.34-0.38 lb ai/A; see Table 4.3a. Total sulfentrazone residues were all <0.15 ppm in/on all treated samples of broccoli.

Table 4.3a. Summary of Residue Data from Broccoli Field Trials with Sulfentrazone.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preplant/preemergence application at a maximum rate of 0.375 lb ai/A									
Sulfentrazone									
Broccoli	0.34-0.38	45-73	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS									
Broccoli	0.34-0.38	45-73	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS									
Broccoli	0.34-0.38	45-73	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total									
Broccoli	0.34-0.38	45-73	12	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Cabbage

A tolerance of 0.20 ppm has been established [40 CFR §180.498(a)(2)] for the combined residues of sulfentrazone and its metabolites HMS and DMS in/on cabbage based on residue data reviewed in PP#1E6311. These data indicate that the combined residues of sulfentrazone, HMS, and DMS) were <0.15-0.18 ppm and <0.15-0.17 ppm in/on cabbage heads with and without wrapper leaves, respectively, harvested 68-104 days following a single ground broadcast application of the 75% DF formulation at 0.375 lb ai/A (1x rate) made 1-3 days prior to transplanting or at the 2- to 4-leaf growth stage (33 days after planting) to direct seeded cabbage. The petition review concluded that two additional cabbage field trials should be conducted in Regions 1 and 8 as a condition for full registration.

Conclusions: The submitted residue data for broccoli along with the previously reviewed data for cabbage are adequate to support the proposed crop subgroup tolerance of 0.20 ppm for residues in/on *Brassica* head and stem, subgroup 5A. Following application of a representative formulation of sulfentrazone at 1x, the combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on broccoli, <0.15-0.18 ppm in/on cabbage heads with wrapper leaves, and <0.15-0.17 ppm in/on cabbage heads without wrapper leaves. As a condition for full registration, HED previously required two additional cabbage field trials to be conducted in Regions 1 and 8. These trials are no longer needed since an adequate number of broccoli and cabbage field trials are available to satisfy geographic representation for head and stem *Brassica*, subgroup 5A.

Brassica, leafy greens, subgroup 5B

Mustard Greens (47311402.der.doc)

The results of the field trials indicate that residues of sulfentrazone were all below the LOQ (<0.05 ppm) in/on all samples of mustard greens harvested 40-66 days following a preemergence broadcast soil application of a 4 lb/gal FlC formulation of sulfentrazone at a rate of ~0.10 lb ai/A (Treatment Plot 2), ~0.20 lb ai/A (Treatment Plot 3) or ~0.40 lb ai/A (Treatment Plot 4); see Table 4.3b. Maximum residues of DMS were 0.098 ppm, 0.136 ppm, and <0.05 ppm in/on mustard green samples from Treatment Plots 2, 3, and 4, respectively. Maximum residues of HMS were 0.051 ppm, 0.162 ppm, and <0.05 ppm in/on mustard green samples from Treatment Plots 2, 3, and 4, respectively. Maximum total residues were 0.198 ppm, 0.291 ppm, and <0.15 ppm in/on mustard green samples from Treatment Plots 2, 3, and 4, respectively.

Table 4.3b. Summary of Residue Data from Mustard Green Field Trials with Sulfentrazone.

Commodity	PHI (days)	Trt Plot No.	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preplant/preemergence application at a maximum rate of 0.375 lb ai/A										
Sulfentrazone										
Mustard greens, leaves	40-66	2	0.092-0.108	14	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.199-0.222	14	<0.05	<0.05	<0.05	<0.05	<0.05	--
		4	0.402	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS										
Mustard greens, leaves	40-66	2	0.092-0.108	14	<0.05	0.098	0.074	<0.05	0.053	0.013
		3	0.199-0.222	14	<0.05	0.136	0.109	<0.05	0.058	0.024
		4	0.402	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS										
Mustard greens, leaves	40-66	2	0.092-0.108	14	<0.05	0.051	0.051	<0.05	<0.050	0.000
		3	0.199-0.222	14	<0.05	0.162	0.148	<0.05	0.070	0.037
		4	0.402	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total										
Mustard greens, leaves	40-66	2	0.092-0.108	14	<0.15	<0.198	0.174	<0.15	0.154	0.013
		3	0.199-0.222	14	<0.15	<0.291	0.248	<0.15	0.178	0.049
		4	0.402	2	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for mustard greens, which is the representative commodity of *Brassica* leafy greens, subgroup 5B, are adequate to fulfill data requirements provided the use directions are revised to indicate a maximum single and seasonal application rate of 0.20 lb ai/A. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500 and the trials conducted reflect the revised proposed use pattern. The residue data for mustard greens indicate that total residues were <0.15 ppm in/on two samples treated at 0.402 lb ai/A (~1.1x). It is noted that higher residues were observed on samples treated at <1.0x. Maximum total residues of <0.198 ppm and <0.291 ppm were reported in/on samples treated at ~0.3x and ~0.5x. The residue data for mustard greens were not entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine the tolerance level as more than half of the samples (8 of 14) had residues that were less then the LOQ (0.05 ppm). HED concludes the data support a tolerance level of 0.40 ppm for free and conjugated residues of sulfentrazone, HMS and DMS in/on *Brassica* leafy greens, subgroup 5B. A revised Section F is required.

Vegetable, Legume, Group 6

Pea, succulent (47311406.der.doc)

The results of the field trials show that residues of sulfentrazone, DMS, and HMS were each below the LOQ (<0.05 ppm) in/on samples of peas (succulent shelled and edible-podded) harvested 52-168 days after a single preemergence broadcast application of a 75% DF formulation of sulfentrazone made to soil at target rates of ~0.1875 lb ai/A (1x; Treatment Plot 2) or ~0.25 lb ai/A (1.3x; Treatment Plot 3); see Table 4.3c. Total sulfentrazone residues were <0.15 ppm in/on all treated samples of succulent shelled and edible-podded peas.

Table 4.3c. Summary of Residue Data from Succulent Pea Field Trials with Sulfentrazone.

Commodity	PHI (days)	Trt No.	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
				n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Proposed Use Pattern: Preemergence application at a maximum rate of 0.1875 lb ai/A										
Sulfentrazone										
Pea, succulent shelled and edible-podded	52-168	2	0.181-0.198	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.242-0.264	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS										
Pea, succulent shelled and edible-podded	52-168	2	0.181-0.198	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.242-0.264	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS										
Pea, succulent shelled and edible-podded	52-168	2	0.181-0.198	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.242-0.264	22	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total										
Pea, succulent shelled and edible-podded	52-168	2	0.181-0.198	22	<0.15	<0.15	<0.15	<0.15	<0.15	--
		3	0.242-0.264	22	<0.15	<0.15	<0.15	<0.15	<0.15	--

HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for succulent peas are adequate to fulfill data requirements. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500, and the trials conducted reflect the proposed use pattern. The field trial data will support a tolerance of 0.15 ppm for residues in/on succulent peas. The combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on mature peas (succulent shelled and edible-podded) following treatment according to the proposed use pattern. A revised Section F is required since the petitioner has proposed a tolerance level of 0.05 ppm for residues in/on mature peas (succulent shelled and edible-podded).

Vegetable, fruiting, group 8

Tomato and Peppers: (47311404.der.doc (includes MRID 47311405))

The crop field studies show that residues of sulfentrazone, DMS, and HMS were each <LOQ (<0.05 ppm) in/on all samples of peppers and tomatoes harvested 19-22 days following the last of two applications (a soil surface, pre-transplant, banded application followed by a postemergence application made between rows with a shielded/hooded sprayer) of either a 4 lb/gal FlC formulation or a 75% DF formulation of sulfentrazone, at total rates of 0.40 lb ai/A (1.1x), 0.50 lb ai/A (1.3x), and 0.75 lb ai/A (2.0x); see Table 4.3d. Total combined residues of sulfentrazone, DMS, and HMS were all <0.15 ppm in/on all treated samples of peppers and tomatoes.

Table 4.3d. Summary of Residue Data from Fruiting Vegetable Field Trials with Sulfentrazone.

Commodity	PHI (days)	Trt Plot No.	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preplant or postemergence application at a maximum seasonal rate of 0.375 lb ai/A										
Sulfentrazone										
Bell Pepper	19-21	2	0.505-0.512	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.739-0.773	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.410	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
		5	0.504-0.507	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.758-0.779	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
Non-bell pepper	19-22	2	0.499-0.505	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.750-0.761	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
Tomato	19-21	2	0.489-1.004	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.730-0.982	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.537	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
	19-21	5	0.490-0.504	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.739-0.758	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS										
Bell Pepper	19-21	2	0.505-0.512	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.739-0.773	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.410	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
		5	0.504-0.507	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.758-0.779	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
Non-bell pepper	19-22	2	0.499-0.505	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.750-0.761	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
Tomato	19-21	2	0.489-1.004	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.730-0.982	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.537	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
	19-21	5	0.490-0.504	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.739-0.758	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS										
Bell Pepper	19-21	2	0.505-0.512	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.739-0.773	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.410	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
		5	0.504-0.507	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.758-0.779	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
Non-bell pepper	19-22	2	0.499-0.505	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.750-0.761	8	<0.05	<0.05	<0.05	<0.05	<0.05	--
Tomato	19-21	2	0.489-1.004	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.730-0.982	28	<0.05	<0.05	<0.05	<0.05	<0.05	--
	21	4	0.537	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
	19-21	5	0.490-0.504	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
		6	0.739-0.758	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total										
Bell Pepper	19-21	2	0.505-0.512	12	<0.15	<0.15	<0.15	<0.15	<0.15	--
		3	0.739-0.773	12	<0.15	<0.15	<0.15	<0.15	<0.15	--
	21	4	0.410	2	<0.15	<0.15	<0.15	<0.15	<0.15	--
		5	0.504-0.507	4	<0.15	<0.15	<0.15	<0.15	<0.15	--
		6	0.758-0.779	4	<0.15	<0.15	<0.15	<0.15	<0.15	--

Table 4.3d. Summary of Residue Data from Fruiting Vegetable Field Trials with Sulfentrazone.

Commodity	PHI (days)	Trt Plot No.	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Non-bell pepper	19-22	2	0.499-0.505	8	<0.15	<0.15	<0.15	<0.15	<0.15	--
		3	0.750-0.761	8	<0.15	<0.15	<0.15	<0.15	<0.15	--
Tomato	19-21	2	0.489-1.004	28	<0.15	<0.15	<0.15	<0.15	<0.15	--
		3	0.730-0.982	28	<0.15	<0.15	<0.15	<0.15	<0.15	--
	21	4	0.537	2	<0.15	<0.15	<0.15	<0.15	<0.15	--
	19-21	5	0.490-0.504	4	<0.15	<0.15	<0.15	<0.15	<0.15	--
		6	0.739-0.758	4	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for peppers (bell and non-bell) and tomatoes are adequate. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500 and the trials conducted reflect the proposed use pattern. The field trial data will support a tolerance of 0.15 ppm for residues in/on fruiting vegetables, crop group 8. Following two applications (a soil surface, pre-transplant, banded application followed by a postemergence application made between rows with a shielded/hooded sprayer) of representative formulations at ~1.1-2.0x, the combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on the representative commodities. A revised Section B is required to remove postemergence uses on the labels since metabolism data are not available to support this use pattern. A revised Section F is also required since the petitioner has proposed a crop group tolerance level of 0.05 ppm.

Okra

Okra residue data were not submitted in support of the proposed use on okra. IR-4 has proposed to translate the existing and submitted fruiting vegetable data (peppers and tomatoes) to okra. The proposed use on okra is identical to the proposed use on the fruiting vegetables crop group. HED has approved adding okra to the fruiting vegetable crop group (see minutes of ChemSAC meeting of 10/18/06). Until 40 CFR §180.41 is updated, a separate tolerance must be established for residues in/on okra.

Conclusions. The available data for the fruiting vegetables, crop group 8 may used to support the proposed tolerance for residues in/on okra. The tolerance should be established at the same level (0.15 ppm) as the fruiting vegetable group tolerance.

Melon subgroup 9A (47311403.der.doc)

The results of the field trials indicate that residues of sulfentrazone, DMS, and HMS were below the LOQ (<0.05 ppm) in/on all samples of cantaloupe harvested 59-94 days after a single broadcast application of a 75% DF formulation of sulfentrazone to soil surface at pre-transplant or preemergence at rates of ~0.20 lb ai/A (Treatment Plot 2), ~0.25 lb ai/A (Treatment Plot 3) or ~0.15 lb ai/A (Treatment Plot 4), with one exception. In one CA trial, residues of HMS were 0.052 ppm in/on cantaloupe samples from Treatment Plot 2. Maximum total residues were <0.152 ppm, <0.15 ppm, and <0.15 ppm in/on cantaloupes from Treatment Plots 2, 3, and 4, respectively. The results of these field trials are summarized in Table 4.3e.

Table 4.3e. Summary of Residue Data from Cantaloupe Field Trials with Sulfentrazone.

Commodity	PHI (days)	Trt No.	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preemergence application at a maximum seasonal rate of 0.25 lb ai/A										
Sulfentrazone										
Cantaloupe, fruit	59-94	2	0.20-0.22	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.25-0.27	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
		4	0.16	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS										
Cantaloupe, fruit	59-94	2	0.20-0.22	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
		3	0.25-0.27	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
		4	0.16	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS										
Cantaloupe, fruit	59-94	2	0.20-0.22	16	<0.05	0.052	0.051	<0.05	<0.05	--
		3	0.25-0.27	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
		4	0.16	2	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total										
Cantaloupe, fruit	59-94	2	0.20-0.22	16	<0.15	<0.152	<0.151	<0.15	<0.15	--
		3	0.25-0.27	16	<0.15	<0.15	<0.15	<0.15	<0.15	--
		4	0.16	2	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for cantaloupes are adequate to support a tolerance of 0.15 ppm for residues in/on the melon subgroup 9A. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500, and the trials conducted reflect the proposed use pattern. Following pre-transplant or preemergence application of a representative formulation at ~0.6-1.0x, the combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on mature cantaloupes. A revised Section F is required since the petitioner has proposed a crop subgroup tolerance level of 0.10 ppm.

Strawberry (47311408.der.doc)

The results of the field trials show that residues of sulfentrazone, DMS, and HMS were each <LOQ (0.05 ppm) in/on all samples of strawberry harvested 56-189 days following a single broadcast soil application of a 75% DF formulation of sulfentrazone made preplant (annual strawberry crops) or during the dormant phase (perennial strawberry crops) at a rate of 0.25-0.26 lb ai/A (Treatment Plot 2) or 0.38-0.40 lb ai/A (Treatment Plot 3); see Table 4.3f. Total sulfentrazone residues were <0.15 ppm in/on all treated samples of strawberry.

Table 4.3f. Summary of Residue Data from Strawberry Field Trials with Sulfentrazone.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preemergence application at a maximum seasonal rate of 0.25 lb ai/A									
Sulfentrazone									
Strawberry	0.25-0.26	56-189	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
	0.38-0.40		16	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS									
Strawberry	0.25-0.26	56-189	16	<0.05	<0.05	<0.05	<0.05	<0.05	--
	0.38-0.40		16	<0.05	<0.05	<0.05	<0.05	<0.05	--

Table 4.3f. Summary of Residue Data from Strawberry Field Trials with Sulfentrazone.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
HMS									
Strawberry	0.25-0.26	56-189	16	<0.05	<0.05	0.05	0.05	<0.05	--
	0.38-0.40		16	<0.05	<0.05	0.05	0.05	<0.05	--
Total									
Strawberry	0.25-0.26	56-189	16	<0.15	<0.15	<0.15	<0.15	<0.15	--
	0.38-0.40		16	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for strawberries are adequate to fulfill data requirements. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500, and the trials conducted reflect the proposed use pattern. The field trial data support a tolerance of 0.15 ppm for residues in/on strawberry. The combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on mature strawberries following a pre-plant or dormant application of a representative sulfentrazone formulation at 1.0-1.6x. A revised Section F is required since the petitioner has proposed a tolerance level of 0.05 ppm for residues in/on strawberries.

Flax: (47311407.de1.doc)

The results of the field trials indicate that residues of sulfentrazone, DMS, and HMS were each <LOQ (0.05 ppm) in/on all samples of flax seed harvested 111-123 days after a single preemergence broadcast soil application of a 75% DF formulation or mixture of two 75% DF formulations of sulfentrazone at a rate of ~0.375 lb ai/A; see Table 4.3g. Total sulfentrazone residues were <0.15 ppm in/on all treated samples of flax seed.

Table 4.3g. Summary of Residue Data from Flax Field Trials with Sulfentrazone.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
Proposed Use Pattern: Preemergence application at a maximum seasonal rate of 0.375 lb ai/A									
Sulfentrazone									
Flax, seed	0.365-0.383	111-123	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
DMS									
Flax, seed	0.365-0.383	111-123	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
HMS									
Flax, seed	0.365-0.383	111-123	12	<0.05	<0.05	<0.05	<0.05	<0.05	--
Total									
Flax, seed	0.365-0.383	111-123	12	<0.15	<0.15	<0.15	<0.15	<0.15	--

[1] HAFT = highest-average field trial. For calculation of the total residues, HAFT, median, and mean, the LOQ value (<0.05 ppm) was used for all residues reported as below the LOQ.

Conclusions: The submitted residue data for flax are adequate to fulfill the data requirements. The number and locations of crop field trials are in accordance with OPPTS Guideline 860.1500, and the trials conducted reflect the proposed use pattern. The field trial data will support a tolerance of 0.15 ppm for residues in/on flax seed. The combined residues of sulfentrazone, DMS, and HMS were <0.15 ppm in/on flax seed following a preemergence application of a representative sulfentrazone formulation at 1.0x. A revised Section F is required since the petitioner has proposed a tolerance for residues in/on flax seed at 0.05 ppm.

A summary of proposed and recommended tolerances for sulfentrazone is presented in Table 4.3h.

Table 4.3h. Tolerance Summary for Sulfentrazone.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Brassica, head and stem, subgroup 5A	0.20	0.20	The established tolerance for cabbage under 180.498(a)(2) should be removed concomitantly when the subgroup 5A tolerance is established
Brassica, leafy greens, subgroup 5B	0.35	0.40	
Melon subgroup 9A	0.10	0.15	
Vegetable, fruiting, group 8	0.05	0.15	
Okra	0.05	0.15	
Pea, succulent	0.05	0.15	
Flax	0.05	0.15	The established time-limited tolerance for flax seed under 180.498(b) should be removed concomitantly when the permanent flax tolerance is established.
Strawberry	0.05	0.15	The established time-limited tolerance for strawberry under 180.498(b) should be removed concomitantly when the permanent strawberry tolerance is established.
Vegetable, tuberous and corm, subgroup 1C	0.15	0.15	Tolerance recommendation is based on residue data translated from potato. The established tolerance for potato under 180.498(a)(2) should be removed concomitantly when the subgroup 1C tolerance is established.

Magnitude of Residues in Livestock

Adequate ruminant and poultry metabolism studies were submitted in conjunction with the soybean petition (PP#4F04407). The metabolism of sulfentrazone in livestock differs from that in plants as metabolism proceeds only by oxidation of the 3-methyl group to form HMS, followed by further oxidation to form sulfentrazone carboxylic acid which is decarboxylated to DMS. Sulfentrazone *per se* and its metabolites HMS and DMS were identified as the residues of concern in meat, milk, poultry and eggs.

HED previously determined that, based on the established sulfentrazone tolerances for soybean and cereal grain commodities and the results of the livestock metabolism studies, conventional feeding studies are not required. This conclusion was reevaluated in conjunction with PP#s 2F6391 and 2E6405 (D287102, 1/10/03, G. Kramer) based on revised dietary burdens resulting from a diet comprised of corn and potato commodities for beef and dairy cattle and corn and rice commodities for poultry. Since a dietary exposure of 10x would not result in quantifiable residues, HED concluded that conventional ruminant and poultry feeding studies were still not required.

In the current petition, the only livestock feedstuff is flax meal. Flax meal is a feed commodity for cattle and swine (10% of diet) and poultry (30% of diet), but would contribute a minor percentage to livestock diets compared to soybeans and cereal grains. Residues of sulfentrazone and its metabolites in/on flax will not result in a higher dietary burden, and tolerances for residues in/on meat, milk, poultry, and egg are not required to support preemergence uses on flax.

Storage Stability

The available storage stability data for sulfentrazone are adequate to support the storage conditions and durations of samples of broccoli, cantaloupe, flax, mustard greens, pea (succulent shelled and edible-podded), pepper, strawberry, and tomato from the submitted crop field trials and the flax and tomato processing studies. There are no storage stability issues and no corrections for storage stability need be applied to the field trial and processing studies.

Processed Food/Feed

Flax 47311407.de2.doc

IR-4 has submitted processing data for sulfentrazone on flax. In one trial conducted in ND during the 2002 growing season, flax seed was harvested 123 days following a single preemergence broadcast soil application of a 75% DF formulation of sulfentrazone at a rate of 0.3718 lb ai/A (~1x), without an adjuvant. The harvested flax seeds were processed into meal and oil using simulated commercial processing procedures.

The processing study indicates that all residues of sulfentrazone, DMS, and HMS were <LOQ (0.05 ppm) in flax seed (RAC), meal, and oil. Since all residues were <LOQ, processing factors could not be calculated. It is noted that no phytotoxic effects were reported following application of the test substance.

The submitted flax processing study is unacceptable for regulatory purposes since the study has not conclusively demonstrated that sulfentrazone residues of concern will not concentrate in flax meal and oil as a result of the proposed use. Quantifiable residues were not detected in the flax seeds used for processing, and the field trial was conducted at only a 1x rate. Since no phytotoxic effects were reported, the flax processing study needs to be repeated using an exaggerated application rate (equal to the maximum theoretical concentration factor for flax or 5x, whichever is less).

Tomato 47311405.der.doc

IR-4 has submitted the results of a tomato processing study with sulfentrazone. Samples used for processing were generated from a field trial conducted in CA during the 2004 growing season. Tomatoes were harvested 20 days following two applications (one banded application to soil surface pre-transplant and one postemergence application between rows using a shielded/hooded sprayer) of a 4 lb/gal FlC formulation of sulfentrazone, applied at rates of ~0.250 lb ai/A/application, for a total rate of ~0.500 lb ai/A (~1.3x; Treatment Plot 2) or at ~0.375 lb ai/A/application, for a total rate of ~0.750 lb ai/A (2.0x; Treatment Plot 3). Applications were made at a 99-day retreatment interval, in 25-31 GPA spray volumes, without an adjuvant. The collected tomato samples were processed into paste and puree using simulated commercial procedures.

The processing study indicates that all residues of sulfentrazone, DMS, and HMS were <LOQ (<0.05 ppm) in/on tomato fruit, paste, and puree. Since all residues were <LOQ, processing factors could not be calculated. The study reported that phytotoxic effects occurred after the first application but the crops fully recovered by the second application. The maximum theoretical concentration factors are 5.5x for processing to tomato paste (OPPTS 860.1520, Table 1).

The submitted tomato processing study is unacceptable since the study does not conclusively demonstrated that sulfentrazone residues of concern will not concentrate in tomato paste and puree as a result of the proposed use. Although the petitioner reported phytotoxic effects after the first application, these plants recovered by the second application. Therefore, an attempt should be made to apply sulfentrazone at an exaggerated rate (equal to the maximum theoretical concentration factor or 5x, whichever is less) to obtain samples with quantifiable residues so that processing factors may be determined.

Field Accumulation in Rotational Crops
Rotational crop studies for corn, rice, sorghum, and wheat were previously submitted in conjunction with the soybean petition (PP#4F04407). Permanent tolerances have been established for indirect or inadvertent residues of sulfentrazone and its metabolites, HMS and DMS, in cereal grains (excluding sweet corn), bran, forage, grain, hay, hulls, stover, and straw as a result of the use on soybeans. As the 1x use rate in soybeans (0.375 lb ai/A) is ≥ the 1x use rate of the proposed new uses, the established tolerances for indirect or inadvertent residues of sulfentrazone and its metabolites, HMS and DMS are adequate to support the subject petition. The proposed rotational crop restrictions are adequate and consistent with previous sulfentrazone petitions.

4.4 International Residue Limits

No Codex, Canadian, or Mexican MRLs have been established for sulfentrazone on the subject crops; therefore, harmonization of MRLs and U.S. tolerances is not an issue at this time.

4.5 Dietary Exposure Analyses

The dietary exposure assessment was completed by HED on 4/3/2009 (Memo, W. Wassell, D362644).

Acute and chronic analyses were performed using DEEM-FCID™ (ver. 2.03). DEEM-FCID™ (ver. 2.03) estimates the dietary exposure of the U.S. population and various population subgroups. The results reported are for the general U.S. Population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, adults 20-49 years old, and adults 50+ years old.

The acute and chronic analysis assumed DEEM™ (ver. 7.81) default processing factors, 100% CT and tolerance-level residues for all commodities. The acute and chronic analysis also incorporated the drinking water estimates provided by EFED. The EDWCs were Tier 1 estimates for groundwater using the SCI-GROW model and surface water using the FIRST model for sulfentrazone and 3-carboxylic acid sulfentrazone. The models utilized an application rate of 0.375 lbs ai/A with 2 applications per season. EDWCs of 0.0358 ppm and 0.026 ppm were used in the acute and chronic analysis, respectively.

The resulting acute food plus water exposure estimates are not of concern to HED (<100% aPAD) at the 95th percentile of the exposure distribution for the U.S. general population (<1% aPAD), and all population subgroups; the most highly exposed population subgroup is all infants with <1% aPAD. As the aPAD is different for females 13 to 49 years old, the resulting acute exposure estimate for females 13 to 49 years old was 13% of the aPAD. See Table 4.5a below for a summary of the results of the acute assessment. The resulting chronic exposure estimates are not of concern to HED. The most highly exposed population was children 1-2 years old utilizing 14% of the cPAD. See Table 4.5b below for a summary of the results of the chronic assessment.

Table 4.5a. Summary of Acute Dietary Exposure and Risk for Sulfentrazone at the 95th Percentile.			
Population Subgroup	aPAD (mg/kg/day)	Exposure (mg/kg/day)	%aPAD
General U.S. Population	2.5 (Endpt. unchanged)	0.004274	<1.0
All Infants (< 1 year old)		**0.009163**	**<1.0**
Children 1-2 years old		0.008026	<1.0
Children 3-5 years old		0.007261	<1.0
Children 6-12 years old		0.005215	<1.0
Youth 13-19 years old		0.003668	<1.0
Adults 20-49 years old		0.003307	<1.0
Adults 50+ years old		0.002915	<1.0
Females 13-49 years old	0.025	0.003180	13

Table 4.5b. Summary of Chronic Dietary Exposure and Risk for Sulfentrazone.			
Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	%cPAD
General U.S. Population	0.025	0.001715	6.9
All Infants (< 1 year old)		0.003023	12
Children 1-2 years old		**0.003449**	**14**
Children 3-5 years old		0.003381	14
Children 6-12 years old		0.002361	9.4
Youth 13-19 years old		0.001639	6.6
Adults 20-49 years old		0.001465	5.9
Adults 50+ years old		0.001329	5.3
Females 13-49 years old		0.001423	5.7

5.0 Residential (Non-Occupational) Exposure/Risk Pathway

This document only presents the assessment of the proposed agricultural uses of sulfentrazone. There are no proposed residential uses at this time; however, there is an existing residential turf use.

5.1 Residential Handler Exposure

Sulfentrazone is registered for use on residential lawns and turf as well golf courses (D289349, M. Dow, 15-May-2003). Sulfentrazone can be applied by professional lawn care operators to residential lawns and to golf courses. No homeowner handler exposure is anticipated from normal application of sulfentrazone.

5.2 Residential Post-application Exposure

Post-application exposure was estimated for toddler hand-to-mouth activity, toddler object-to-mouth activity, toddler dermal contact and adult dermal contact to treated residential turf. All residential dermal and incidental oral exposure and risk estimates are below HED's level of concern (MOEs ≥100). A post-application exposure assessment was conducted for adult and adolescent golfers. Likewise, dermal exposure and risk estimates for golfers are below HED's level of concern (MOEs ≥100).

Table 5.2. Residential Post-Application Exposure and Risk Estimates from Contacting Turf Treated with Sulfentrazone.

Activity	TTR[2] ($\mu g/cm^2$)	PDR[3] (mg/kg/day)	MOE[4]
Toddler Hand to Mouth	0.017	4.5×10^{-4}	31,000
Toddler Object to Mouth	0.067	2.2×10^{-4}	64,000
Toddler Dermal contact	0.017	1.18×10^{-2}	8,500
Adult Dermal contact	0.017	8.2×10^{-3}	12,000

1. SOPs for Residential Exposure Assessments, Draft, 17 DEC 97, and ExpoSAC Policy No. 11, 22 FEB 01- Recommended Revisions to the SOPs for Residential Exposure.
2. TTR = Turf Transferable Residue = Application rate (0.03 lb ai/A) * 5% x (4.54×10^8 µg/lb ai) x (2.47×10^{-8} A/cm^2).
3. Potential Dose Rate (PDR):
   Hand to mouth = (TTR x 50% saliva extraction x 20 cm^2/event x 20 events/hr x 10^{-3} mg/µg x 2 hr/day/15 kg).
   Object to mouth = (TTR x 25 cm^2/day x 10^{-3} mg/µg x 2 hr/day)/15 kg.
   Dermal = (TTR x 10^{-3} mg/µg x TC (cm^2/hr) x 2 hr/day ÷ 60 kg for adults and 15 kg for toddlers.
   TC for adult = 14,500 cm^2/hr and for toddler = 5,200 cm^2/hr.
4. MOE = Margin of Exposure = NOAEL ÷ PDR In this case short and intermediate term dermal NOAEL = 100 mg/kg/day; incidental oral NOAEL = 14 mg/kg/day.

A combined MOE for toddler hand-to-mouth + toddler object-to-mouth + toddler dermal post-application exposures is 6,000 and is expressed as: $1/[(1/MOE_{HtM}) + (1/MOE_{OtM}) + (1/MOE_{Dermal})]$.

Adult and Adolescent Golfer Post-Application Dermal Exposure

Golfer post-application exposure may be estimated using the convention stated in ExpoSAC draft Policy regarding "Golfer Exposure Assessment for Adults and Children" (24 August 2000). The draft policy states that adult and adolescent golfer dermal post-application exposure may be calculated as:

DE(t) (mg a.i./kg bw/day) = (TTR(t) (µg/cm^2)) * TC (cm^2/hr) * hr/day/1000 µg/mg * BW (body weight (kg)).

Where:

DE(t)	=	dermal exposure at time (t) attributable to golfing on previously treated turf (mg a.i./kg bw/day).
TTR(t)	=	turf transferable residue at time t (µg/cm^2) (lacking data assumed to be 5 % application rate or 0.05 x 0.03 lb/A).
TC	=	Transfer Coefficient (500 cm^2/hr).
Hr	=	exposure period (4 hours).
BW	=	body weight (kg) (70 kg for adult; adjusted (multiplied) by a factor of 1.7 for child golfers)) A BW of 60 kg is utilized if the toxicological endpoint is derived from a developmental study and there are fetal effects.

Therefore,

DE = 0.03 x 0.05 = 0.0015 μg/cm² * 500 cm²/hr * 4 hr/day/1000μg/mg ÷ 60 kg bw = 0.00005 mg a.i./kg bw/day.

MOE for adult golfer is 100 mg a.i./kg bw/day ÷ 0.00005 mg a.i./kg bw/day = 2,000,000.

The adult dose level is adjusted by a factor of 1.7 to estimate child golfer exposure therefore 0.00005 mg a.i./kg bw/day * 1.7 = 0.000085 mg a.i./kg bw/day.

MOE for child golfer is 100 mg a.i./kg bw/day ÷ 0.000085 = 1,200,000.

An MOE ≥100 is sufficient to protect adults and toddlers from post-application exposure to residential turf and to protect adult and adolescent golfers from post-application exposure to treated golf courses. Since the short- and intermediate-term toxicological endpoints are the same, the estimates of short- and intermediate-term risk are the same. In this case, all MOEs for post-application exposure to treated residential turf and to treated golf course turf, are >100 and therefore are not of concern to HED.

5.3 Other (Spray Drift)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method additionally employed for sulfentrazone. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT® computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

6.0 Aggregate Risk Assessments and Risk Characterization

Acute and chronic aggregate risks are made up only of dietary sources; therefore, the exposure estimates provided in the dietary exposure analysis represent acute and chronic aggregate exposure, respectively. Short- and intermediate-term aggregate risks are made up of dietary and non-dietary sources of exposure. Since sulfentrazone is proposed for use on turf, post-application residential exposure is expected. Only short-term aggregate risk was estimated since the use pattern is not expected to result in exposure of more than a 30-day duration. Short-term aggregate risk is made up of average dietary exposures from food and drinking water sources plus dermal and oral (children only) residential exposures. Dietary (food and drinking water) exposure is based on a Tier 1 chronic dietary exposure assessment. An aggregate cancer risk assessment was not performed because sulfentrazone is not considered to be a carcinogen.

6.1. Short-Term Aggregate Risk

Short-term exposures exist for adults and children from the registered turf application use. For short-term exposures, incidental oral and dermal exposure risk assessments are appropriate to aggregate due to similarities in the toxicity endpoints observed between the oral and dermal routes. The short-term incidental oral and dermal exposures are combined with chronic dietary (food and water) exposure for determination of aggregate short-term exposures. HED uses chronic dietary exposure when conducting short-term aggregate assessments as they have determined that these will more accurately reflect exposure from food over the HED defined short-term interval (1-30 days) than will acute exposure.

For adults, there is no significant incidental oral exposure; therefore, only dermal exposure was appropriate to aggregate with dietary (food) and water. For young children, due primarily to their hand-to-mouth activities, oral (non-dietary) and dermal exposures were aggregated with dietary (food) and water. Children can be exposed to the following three post-application scenarios: 1) post-application exposure from the incidental ingestion (hand-to-mouth) from contacting treated turf; 2) post-application exposure from the incidental ingestion (object-to-mouth) from contacting treated turf; and 3) post-application dermal exposure from contact with treated turf. Table 6.1 summarizes the short-term aggregate exposures and risk estimates for toddlers and adults. Since the aggregate MOEs are ≥ 100, short-term aggregate exposures to sulfentrazone are not of concern to HED.

Table 6.1. Short- and Intermediate-term Aggregate Risk

Population	Target MOE	Background Dietary + Incidental Oral Exposures			Residential Exposures		Aggregate MOE (food, water, and residential)[d]
		Chronic Food and Water Exposure (mg/kg/day)	Incidental Oral Exposure (mg/kg/day)[a]	Oral MOE[b]	Dermal Exposure (mg/kg/day)	Dermal MOE[c]	
General U.S. Population	100	0.001715	N/A	8,200	0.00825	12,000	4,900
Children 1-2 years old		0.003449	0.00067	3,400	0.0118	8,500	2,400

a. Incidental Oral Exposure = Hand-to-Mouth exposure + Object-to-Mouth exposure
b. Oral MOE = NOAEL (14 mg/kg/day) ÷ (chronic food/water exposure + incidental oral exposure).
c. Dermal MOE = NOAEL (100 mg/kg/day) ÷ (dermal exposure).
d. Aggregate MOE = 1/[(1/oral MOE) + (1/dermal)].

7.0 Cumulative Risk Characterization/Assessment

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 sulfentrazone and any other substance and sulfentrazone does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that sulfentrazone does not have 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 Pathway

The occupational exposure and risk assessment was performed by HED (Memo, K. Lowe, 4/7/09; DP#: 362643). The proposed use is on head and stem *Brassica*, leafy green *Brassica*, melons, fruiting vegetables, okra, succulent peas, flax, strawberry, and tuberous and corm vegetables, and also impregnation to dry bulk fertilizer and application with dry fertilizer. Occupational exposure is possible for individuals that handle the end-use products and/or for individuals that may enter treated areas. Therefore, occupational handler and post-application exposure was assessed.

8.1 Occupational Handler Exposure

Sulfentrazone can be applied to the soil aerially, by chemigation, or using groundboom equipment. To impregnate sulfentrazone on dry bulk fertilizer, the product label recommends that a closed rotary-drum mixer or other commonly used dry bulk fertilizer blender equipped with suitable spray equipment be used. A slurry of the product is prepared and added to the impregnation spray tank. Once impregnated on the dry-bulk fertilizer, it is applied by dry fertilizer spreader equipment. It is anticipated that the following scenarios could result in handler exposure:

- Mixing/loading liquids to support aerial applications,
- Mixing/loading liquids to support chemigation applications,
- Mixing/loading liquids to support groundboom applications,
- Mixing/loading water-dispersible granules to support aerial applications,
- Mixing/loading water-dispersible granules to support chemigation applications,
- Mixing/loading water-dispersible granules to support groundboom applications,
- Applying sprays with aircraft,
- Applying sprays with groundboom equipment,
- Flagging to support aerial spray applications,
- Impregnating liquids onto dry bulk fertilizer in commercial settings,
- Impregnating liquids onto dry bulk fertilizer on farm,
- Impregnating water-dispersible granules onto dry bulk fertilizer in commercial settings,
- Impregnating water-dispersible granules onto dry bulk fertilizer on farm,
- Applying impregnated dry bulk fertilizer with commercial equipment, and
- Applying impregnated dry bulk fertilizer with grower-owned equipment.

No chemical-specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (August, 1998). There are no data to assess impregnating liquids or water-dispersible granules onto dry bulk fertilizer in commercial settings. The assumptions that the amount of sulfentrazone handled per day in commercial settings (500 – 960 tons) make it unlikely that open mixing/loading is used for this use. Therefore, as a reasonable surrogate for impregnation of dry bulk fertilizer in commercial settings, unit exposure values from PHED for engineering controls (closed mixing/loading) are used. The only current engineering control for closed mixing/loading of water-dispersible granules is water-soluble packaging; however, these data are only used as a surrogate since no other data are available. The use of this data does not require that the sulfentrazone product be re-formulated.

For pesticide handlers, HED presents estimates of dermal exposure for "baseline" (i.e., workers wearing a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus

socks and no protective gloves), as well as for "baseline" and the use of protective gloves or other personal-protective equipment (PPE), as might be necessary. The sulfentrazone product labels direct applicators and other handlers to wear a long-sleeve shirt, long pants, chemical-resistant gloves and shoes plus socks.

Handler exposure is expected to be short- or intermediate-term based on information provided on proposed labels. In addition, the short- and intermediate-term toxicological endpoints are the same; therefore, the estimates of risk for short-term duration exposures are protective of those for intermediate-term duration exposures. Long-term exposures are not expected; therefore, a long-term assessment was not conducted. The average adult body weight of 60 kg was used for estimating dermal and inhalation dose, since the toxicological effects are female-specific.

Tables 8.1a and 8.1b present the estimated risks for workers based on the short- and intermediate-term dermal and inhalation exposures wearing baseline PPE. HED has determined that risks are not of concern (i.e., MOEs $\geq$100 for dermal and $\geq$1000 for inhalation), provided workers wear protective gloves as recommended on the label.

It should be noted that only engineering control data are available to assess dermal and inhalation risks to handlers operating aircraft (enclosed cockpit) and to commercial handlers participating in dry bulk fertilizer impregnation (closed mixing/loading/application systems). The risks are not of concern for pilots using enclosed cockpits and for commercial handlers involved in dry bulk fertilizer impregnation using closed mixing/loading/application systems and wearing baseline attire. The only current engineering control for closed mixing/loading of water-dispersible granules is water-soluble packaging, however, these data are only used as a surrogate since no other data are available. The use of this data does not require that the sulfentrazone product be re-formulated.

Table 8.1a. Agricultural Handler Exposure and Risk for Sulfentrazone.

Exposure Scenario	Crop or Target	App Rate[a] (lb ai/A)	Acres Treated Daily[b]	Unit Exposure[c]			Dose (mg/kg/day)			MOEs		
				Baseline Dermal mg/lbai	PPE-G Dermal mg/lb ai	Baseline Inhalation µg/lb ai	Baseline Dermal[d,h]	PPE-G Dermal[i]	Baseline Inhalation[e]	Baseline Dermal[f]	PPE-G Dermal	Baseline Inhalation[g]
Mixer/Loader												
Mixing/Loading Liquid Concentrates for Aerial Applications	flax	0.375	1200	2.9	0.023	1.2	22	0.17	0.009	**5**	580	2,800
	Brassica, head and stem; *Brassica*, leafy green; and strawberry	0.375	350				6.3	0.05	0.0026	**16**	2,000	9,500
	vegetables, tuberous and corm; and melons	0.25	350				4.2	0.034	0.0018	**24**	3,000	14,000
Mixing/Loading Liquid Concentrates for Chemigation Applications	*Brassica*, head and stem; *Brassica*, leafy green; strawberry and flax	0.375	350	2.9	0.023	1.2	6.3	0.05	0.0026	**16**	2,000	9,500
	vegetables, tuberous and corm; and melons	0.25	350				4.2	0.034	0.0018	**24**	3,000	14,000
	succulent peas	0.188	350				3.2	0.025	0.0013	**31**	4,000	19,000
Mixing/Loading Liquids Concentrates for Groundboom Applications	flax	0.375	200	2.9	0.023	1.2	3.6	0.029	0.0015	**28**	3,500	17,000
	Brassica, head and stem; *Brassica*, leafy green; fruiting vegetables; okra; and strawberry	0.375	80				1.5	0.012	0.0006	**69**	8,700	42,000
	vegetables, tuberous and corm; and melons	0.25	80				0.97	0.0077	0.0004	100	13,000	63,000
	succulent peas	0.188	80				0.73	0.0058	0.0003	140	17,000	83,000

Table 8.1a. Agricultural Handler Exposure and Risk for Sulfentrazone.

Exposure Scenario	Crop or Target	App Rate[a] (lb ai/A)	Acres Treated Daily[b]	Unit Exposure[c]			Dose (mg/kg/day)			MOEs		
				Baseline Dermal mg/lbai	PPE-G Dermal mg/lb ai	Baseline Inhalation µg/lb ai	Baseline Dermal[d,h]	PPE-G Dermal[i]	Baseline Inhalation[e]	Baseline Dermal[f]	PPE-G Dermal	Baseline Inhalation[g]
Mixing/Loading Water-Dispersible Granules for Aerial Applications	flax	0.375	1200	0.066	0.066	0.77	0.5	0.5	0.0058	200	200	4,300
	Brassica, head and stem; *Brassica*, leafy green; strawberry	0.375	350				0.14	0.14	0.0017	690	690	15,000
	vegetables, tuberous and corm; and melons	0.25	350				0.096	0.096	0.0011	1,000	1,000	22,000
Mixing/Loading Water-Dispersible Granules for Chemigation Applications	*Brassica*, head and stem; *Brassica*, leafy green; strawberry; and flax	0.375	350	0.066	0.066	0.77	0.14	0.14	0.0017	690	690	15,000
	vegetables, tuberous and corm; and melons	0.25	350				0.096	0.096	0.0011	1,000	1,000	22,000
	succulent peas	0.188	350				0.072	0.072	0.00084	1,400	1,400	30,000
Mixing/Loading Water-Dispersible Granules for Groundboom Applications	flax	0.375	200	0.066	0.066	0.77	0.083	0.083	0.00096	1,200	1,200	26,000
	Brassica, head and stem; *Brassica*, leafy green; fruiting vegetables; okra; strawberry	0.375	80				0.033	0.033	0.00039	3,000	3,000	65,000
	vegetables, tuberous and corm; and melons	0.25	80				0.022	0.022	0.00026	4,500	4,500	97,000
	succulent peas	0.188	80				0.017	0.017	0.00019	6,000	6,000	130,000
Applicator												

Table 8.1a. Agricultural Handler Exposure and Risk for Sulfentrazone.

Exposure Scenario	Crop or Target	App Rate[a] (lb ai/A)	Acres Treated Daily[b]	Unit Exposure[c]			Dose (mg/kg/day)			MOEs		
				Baseline Dermal mg/lbai	PPE-G Dermal mg/lb ai	Baseline Inhalation µg/lb ai	Baseline Dermal[d,h]	PPE-G Dermal[i]	Baseline Inhalation[e]	Baseline Dermal[f]	PPE-G Dermal	Baseline Inhalation[g]
Applying Sprays via Aerial Equipment[j]	flax	0.375	1200	0.005 (eng. control)	No Data	0.068 (eng. control)	0.038 (eng cntl)	No Data	0.00051 (eng cntl)	2,700 (eng cntl)	No Data	49,000 (eng cntl)
	Brassica, head and stem; *Brassica*, leafy green; strawberry	0.375	350				0.011 (eng cntl)	No Data	0.00015 (eng cntl)	9,100 (eng cntl)	No Data	170,000 (eng cntl)
	vegetables, tuberous and corm; and melons	0.25	350				0.0073 (eng cntl)	No Data	0.000099 (eng cntl)	14,000 (eng cntl)	No Data	250,000 (eng cntl)
Applying Sprays via Groundboom Equipment	flax	0.375	200	0.014	0.014	0.74	0.018	0.018	0.00093	5,700	5,700	27,000
	Brassica, head and stem; *Brassica*, leafy green; fruiting vegetables; okra; strawberry	0.375	80				0.007	0.007	0.00037	14,000	14,000	68,000
	vegetables, tuberous and corm; and melons	0.25	80				0.0047	0.0047	0.00025	21,000	21,000	100,000
	succulent peas	0.188	80				0.0035	0.0035	0.00019	28,000	28,000	130,000
Flagger												
Flagging for Aerial Sprays Applications	*Brassica*, head and stem; *Brassica*, leafy green; strawberry; and flax	0.375	350	0.011	NA	0.35	0.024	NA	0.00077	4,200	NA	33,000
	vegetables, tuberous and corm; and melons	0.25	350				0.016	NA	0.00051	6,200	NA	49,000

a. Application Rates based on proposed uses on registered labels for sulfentrazone products EPA 379-3189 and 379-3220 and Revised Section B for these labels.
b. ExpoSAC Policy # 9.1
c. Unit Exposures based on PHED Version 1.1. Engineering control unit exposure for applying sprays via aerial equipment = closed cockpit.
d. Dermal Dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x acres treated / body weight (60 kg adult female).
e. Inhalation Dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x acres treated * inhalation absorption (100%) / body weight (60-kg adult female).
f. Dermal MOE = NOAEL (100 mg/kg/day) / dermal daily dose (mg/kg/day). Level of concern = 100.
g. Inhalation MOE = LOAEL (25 mg/kg/day) / inhalation daily dose (mg/kg/day). Level of concern = 1000.
h. Baseline Dermal: Long-sleeve shirt, long pants, and no gloves; Baseline Inhalation: no respirator.
i. Baseline plus Gloves Dermal: Baseline plus chemical-resistant gloves.

Table 8.1b. Agricultural Handler Exposure and Risk for Sulfentrazone – Dry Bulk Fertilizer Preparation.

Exposure Scenario	App Rate[a] (lb ai/A)	Amt Handled Daily[b]	Unit Exposure[c]			Dose (mg/kg/day)			MOEs		
			Baseline Dermal mg/lb ai	PPE-G Dermal mg/lb ai	Baseline Inhalation µg/lb ai	Baseline Dermal[d,h]	PPE-G Dermal[i]	Baseline Inhalation[e]	Baseline Dermal[f]	PPE-G Dermal	Baseline Inhalation[g]
Mixer/Loader											
Mixing/Loading Liquids for Commercial Impregnation of Dry Bulk Fertilizers (PHED)	3.75 lb ai/ton	960 tons	0.0086 (eng cntl)	No Data	0.083 eng cntl	0.52 eng cntl	No Data	0.005 eng cntl	190 eng cntl	No Data	5,000 eng cntl
		500 tons		No Data		0.27 eng cntl	No Data	0.0026 eng cntl	370 eng cntl	No Data	9,600 eng cntl
Mixing/Loading Liquids for On-farm Impregnation of Dry Bulk Fertilizers (PHED)	0.375 lb ai/acre	160 acres	2.9	1.2	0.023	2.9	0.023	0.0012	34	4,300	21,000
		80 acres				1.5	0.0115	0.0006	69	8,700	42,000
Mixing/Loading Dry Flowables for Commercial Impregnation of Dry Bulk Fertilizers (PHED)	3.75 lb ai/ton	960 tons	0.0098 (eng cntrl)	No Data	0.24 eng cntrl	0.59 eng cntl	No Data	0.014 eng cntl	170 eng cntl	No Data	1,700 eng cntl
		500 tons				0.31 eng cntl	No Data	0.0075 eng cntl	330 eng cntl	No Data	3,300 eng cntl
Mixing/Loading Dry Flowables for On-farm Impregnation of Dry Bulk Fertilizers (PHED)	0.375 lb ai/acre	160 acres	0.066	0.77	0.066	0.066	0.066	0.00077	1,500	1,500	32,000
		80 acres				0.033	0.033	0.00039	3,000	3,000	65,000
Applicator											
Commerical Application of Dry Bulk Fertilizers using PHED tractor-drawn granular spreader data)	0.375 lb ai/acre	320 acres	0.0099	1.2	0.0072	0.02	0.0144	0.0024	5,100	6,900	10,000
On-farm Applications of Dry Bulk Fertilizers (using PHED tractor-drawn granular spreader data)		160 acres				0.0099	0.0072	0.0012	10,000	14,000	21,000
		80 acres				0.005	0.0036	0.0006	20,000	28,000	42,000

a. Application Rates based on proposed uses on registered labels for sulfentrazone products EPA 379-3189 and 379-3220.
b. Industry input and professional judgment.
c. Unit Exposures based on PHED Version 1.1.

d. Dermal Dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre or lb ai/ton) x acres that will be treated or tons fertilizer treated / body weight (60 kg adult female).
e. Inhalation Dose (mg/kg/day) = daily unit exposure (mg/ lb ai) x application rate (lb ai/acre) x acres treated x inhalation absorption (100%) / body weight (60-kg adult female).
f. Dermal MOE = NOAEL (100 mg/kg/day) / dermal daily dose (mg/kg/day). Level of concern = 100.
g Inhalation MOE = LOAEL (25 mg/kg/day) / inhalation daily dose (mg/kg/day). Level of concern = 1000.
h. Baseline Dermal: Long-sleeve shirt, long pants, and no gloves; Baseline Inhalation: no respirator. Engineering Control dermal and inhalation: closed mixing system
i. Baseline plus Gloves Dermal: Baseline plus chemical-resistant gloves.

8.2 Occupational Post-application Exposure

HED assumes that inhalation exposures are minimal following outdoor applications of an active ingredient with low vapor pressure. Since sulfentrazone is applied only in outdoor settings and has a low vapor pressure, post-application inhalation exposures and risks were not assessed.

Most of the proposed uses for sulfentrazone are soil-directed preplant or preemergent uses where no crop foliage is present. Currently, HED has no transfer coefficients or other data to assess post-application dermal exposures to soil by occupational workers. In general, such exposures are considered to be negligible. Therefore, for the proposed soil-directed uses, post-application exposures and risks to occupational workers were not assessed. One proposed use is for a postemergent application between the rows of fruiting vegetables and okra using ground equipment with shields or hoods to protect the crop foliage from exposure. Even though HED is not supporting the postemergent use based on the unavailability of metabolism data, post-application worker exposure and risk were assessed for this proposed use. This assessment is considered to be a Tier I, screening-level estimate, demonstrating that there are minimal potential risks to workers re-entering fields treated with postemergent applications of sulfentrazone.

Since no post-application data were submitted in support of this registration action, dermal exposures during post-application activities were estimated using dermal transfer coefficients from the ExpoSAC Policy Number 3.1: Agricultural Transfer Coefficients, August 2000, summarized in Table 8.2a below and the following assumptions:

- Application Rate = 0.375 lb ai/A for fruiting vegetable and okra applications
- Exposure Duration = 8 hours per day
- Body Weight = 60 kg for adult female
- Dermal Absorption = 100%
- Fraction of a.i. retained on foliage is assumed to be 20% (0.2) on day zero (= % dislodgeable foliar residue, DFR, after initial treatment) for agricultural crops. This fraction is assumed to further dissipate at the rate of 10% (0.1) per day on following days. These are default values established by HED's ExpoSAC.

Table 8.2a. Anticipated Post-application Activities and Dermal Transfer Coefficients.

Proposed Crops	Policy Crop Group Category	Transfer Coefficients (cm^2/hr)	Activities
Eggplant, Groundcherry, Pepino, Pepper (includes bell pepper, chili pepper, pimento, sweet pepper), Tomatillo, Tomato and Okra	Vegetables, Fruiting	700	Scouting, Thinning, Irrigation

The post-application exposure associated with the proposed new use is summarized in Table 8.2b. The resulting MOE is greater than 100 on day 0 (12 hours after application) and, therefore, does not exceed HED's LOC.

Table 8.2b. Post-application Exposure and Risk for Sulfentrazone.				
Crop Grouping/Crop	Days after Treatment	DFR[1] (μg/cm^2)	Daily Dermal Dose[2] (mg/kg/day)	MOE[3]
Fruiting Vegetables and Okra	0 (12 hours)	0.84	0.079	1,300

1 = DFR = Dislodgeable Foliar Residue = application rate (lb ai/A) x (1- daily dissipation rate) t x 4.54E8 μg/lb x 24.7E-9 A/cm^2 x 20% DFR after initial treatment.
2 = Daily Dermal Dose = [DFR (μg/cm^2) x Tc (700 cm2/hr) x 0.001 mg/μg x 8 hrs/day] / body weight (60-kg adult female).
3 = MOE = NOAEL/Daily Dose (Adult Dermal NOAEL = 100 mg/kg/day).

REI: Since post-application risks were not a concern on day 0 (12 hours following application), the REI is based on the acute toxicity of sulfentrazone technical material which is classified as Category III for acute dermal toxicity and for eye irritation potential and Category IV for skin irritation potential. Sulfentrazone is not a dermal sensitizer. Under the Worker Protection Standard for Agricultural Pesticides, active ingredients classified as acute toxicity categories III or IV for these routes are assigned a 12-hour REI. Therefore, the 12-hour REI that appears on the proposed label is adequate.

9.0 Data Needs and Label Recommendations

9.1 Toxicology

* **Immunotoxicity Study.** An immunotoxicity study is now a data requirement in the 40 CFR revised Part 158.

9.2 Residue Chemistry

* Revised Section B (for conditional registration).
* Revised Section F (for conditional registration).
* As the reference standard for the metabolite HMS has expired 4/1/2008, the petitioner must submit a new standard (for conditional registration). If new standards are being submitted, they should be sent to the ACL, which is located at Fort Meade, to the attention of Theresa Cole at the following address:

  USEPA
  National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
  701 Mapes Road
  Fort George G. Meade, MD 20755-5350

* For a permanent registration, flax and tomato processing studies should be submitted. Since phytotoxicity does not appear to be an issue, the requested processing studies should use an exaggerated application rate (equal to the maximum theoretical concentration factor or 5x, whichever is less).

9.3 Occupational and Residential Exposure

* None

Attachment 1: Sulfentrazone Toxicity Profile Tables.

Acute Toxicity Profile – Sulfentrazone.				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral [rat]	41911605	LD_{50} = 2855 (M & F) mg/kg	III
870.1200	Acute dermal [mice]	41911606	LD_{50} = 711 (M & F) mg/kgLD50 = 711 (M & F) mg/kg	III
870.1200	Acute dermal	41911606 42286400	LD50 > 2000 mg/kg/day	III
870.1300	Acute inhalation [rat]	42471002	4-hour, whole body exposure; LC50 > 4.13 mg/L	III
870.2400	Acute eye irritation [rabbit]	41911608	Corneal opacity, iritis, diffuse irritation within 24, clearing by day 4	III
870.2500	Acute dermal irritation [rabbit]	41911609	Non-irritating	IV
870.2600	Skin sensitization [Guinea Pig]	41911610	Not a Dermal Sensitizer	N/A

Toxicity Profile for Sulfentrazone.

Guideline No./Study Type	MRID No. (year)/Classification/ Doses	Results
870.3100 90-Day oral toxicity (rat)	43004601 (1990) Acceptable/Guideline 0, 300, 1000, 3000, & 7000 ppm, M: 0, 3.3, 6.7, 19.9, 65.8, 199.3 & 534.9 mg/kg/day F: 0, 4, 7.7, 23.1, 78.1, 230.5 & 404.3 mg/kg/day	Systemic Toxicity NOAEL = 19.9 mg/kg/day in males and 23.1 mg/kg/day in females Systemic Toxicity LOAEL= 65.8 mg/kg/day in males and 78.1 mg/kg/day in females, based on clinical signs of anemia (reduced hematocrit, hemoglobin, mean cell volume, and mean cell hemoglobin values during treatment).
870.3100 90-Day oral toxicity (mice)	43616517 (1993) Acceptable/Guideline 0, 50, 100, 300, 550, 1000 & 3000 ppm M: 0, 10.3, 17.8, 60, 108.4, & 194.4 mg/kg/day F: 0, 13.9, 29, 79.8, 143.6, & 257 mg/kg/day	Systemic Toxicity NOAEL = 60 mg/kg/day in males and 79.8 mg/kg/day in females Systemic Toxicity LOAEL= 108.4 mg/kg/day in males and 143.6 mg/kg/day in females, based on decreased body weights, body-weight gains, red blood cells, hemoglobin, hematocrit, and severity of splenic micropathology (increased incidence and severity of extramedullary hematopoiesis). 4-week recovery period reversed all the treatment related effects except extramedullary hematopoiesis; however severity was reduced.

Guideline No./Study Type	MRID No. (year)/Classification/ Doses	Results
870.3150 90-Day oral toxicity (dog)	42932102 (1992) Acceptable/Guideline 0, 300, 800 & 2000 ppm M/F: 0/0, 10/10, 28/28 & 57/73 mg/kg/day	Systemic Toxicity NOAEL= 28 mg/kg/day for males and females Systemic Toxicity LOAEL= 57/73 mg/kg/day (M/F), based on decreased body weights (7-10%) and body-weight gains during first 5 weeks of study; decreased hemoglobin, hematocrit, mean cell volume, mean cell hemoglobin and mean cell hemoglobin concentration, and increased absolute liver weights and alkaline phosphatase levels, and microscopic changes in the liver and spleen (pigmented sinusoidal microphages in the liver, swollen centrilobular hepatocytes and pigmented reticuloendothelial cells in the spleen).
870.3200 21-Day dermal toxicity (rabbit)	44248301 (1996) Acceptable/Guideline 0, 10, 30, 100, 300 & 1000 mg/kg/day	Systemic and Dermal Toxicity NOAEL = 1000 mg/kg/day (HDT) Systemic and Dermal Toxicity LOAEL was not established.
870.3700a Prenatal Developmental (rat)	42932104 (1992) Acceptable/Guideline 0, 1, 10, 25 & 50 mg/kg/day	Maternal NOAEL = 25 mg/kg/day Maternal LOAEL= 50 mg/kg/day, based upon increased relative splenic extramedullary hematopoiesis Developmental NOAEL = 10 mg/kg/day Developmental LOAEL = 25 mg/kg/day, based upon decreased mean fetal weights, and retardation in skeletal development evidenced by an increased number of litters with any variation and by decreased number of caudal vertebral and metacarpal ossification sites.
870.3700 Prenatal developmental (rat)	43651003 (1992) Acceptable/Non-Guideline 0, 25, & 50 mg/kg/day Study was conducted to evaluate external and cardiac abnormalities	Maternal NOAEL = 25 mg/kg/day Maternal LOAEL =50 mg/kg/day, based on decreased mean body weights during gestation, and decreased litter size. Developmental NOAEL = 25 mg/kg/day Developmental LOAEL = 50 mg/kg/day, based on significant reductions in the number of implantations and percentage of live fetuses, increase in the percentage of early resorptions, and decreased fetal body weights. Supplemental study to the 1992 Developmental-Toxicity Study in Rats (MRID 42932104)
870.3700 Prenatal dermal developmental (rat)	MRID 42932105 (1992) Acceptable/Guideline 0, 5, 25, 50, 100, & 250 mg/kg/day	Maternal NOAEL > 250 mg/kg/day Maternal LOAEL was not established Developmental NOAEL = 100 mg/kg/day Developmental LOAEL= 250 mg/kg/day, based on decreased fetal body weight; increased incidence of fetal variations: hypoplastic or wavy ribs, incompletely ossified lumbar vertebral arches, and incompletely ossified ischia or pubis; and reduced number of thoracic vertebral and rib ossification sites.

Guideline No./Study Type	MRID No. (year)/Classification/ Doses	Results
870.3700b Prenatal Developmental (rabbit)	MRID 42932106 (1993) Acceptable/Guideline 0, 100, 250, & 375 mg/kg/day	Maternal NOAEL = 100 mg/kg/day Maternal LOAEL = 250 mg/kg/day, based on increased abortions, clinical signs (hematuria and decreased feces), and reduced body-weight gain Developmental NOAEL = 100 mg/kg/day Developmental LOAEL = 250 mg/kg/day, based on increased resorptions, decreased live fetuses per litter, and decreased fetal weights.
870.3800 2-Generation reproduction and fertility effects (rat)	43345408 (1994) Acceptable/Guideline 0, 200, 500, & 700 ppm M/F: 0, 14/16, 33/40, & 46/56 mg/kg/day	Parental Toxicity NOAEL =14 (M) and 16 (F) mg/kg/day Parental Toxicity LOAEL = 33 (M) and 40 (F) mg/kg/day based on decreased maternal body weight/body-weight gain during gestation in both generation (P & F1) and reduced premating body-weight gain in second generation (F1) males. Reproductive Toxicity NOAEL = 14 (M) and 16 (F) mg/kg/day Reproductive Toxicity LOAEL =33 (M) and 40 (F) mg/kg/day, based on increased duration of gestation in females and degeneration and/or atrophy of the germinal epithelium of the testes and oligospermia and intratubular degenerated seminal material in the epididymis of F1 males. Offspring Toxicity NOAEL=14 (M) and 16 (F) mg/kg/day Offspring Toxicity LOAEL= 33 (M) and 40 (F) mg/kg/day, based on reduced prenatal viability (fetal & litter), reduced litter size, increased no. of stillborn pups, reduced pup and litter postnatal survival and decreased pup body weights throughout lactation.
870.3800 1-Generation reproduction and fertility effects (rat)	43869101(1995) Acceptable/Nonguideline 0, 50, 100, 200, & 500 ppm F0 M/F: 0, 3.9/4.1, 7.8/13.4, 16/16 & 40/43 mg/kg/day F1 M/F: 0/0, 4.5/5.0, 9.2/10.1, 18/20 & 45/51 mg/kg/day	Systemic/Developmental Toxicity NOAEL =20 (F) mg/kg/day Systemic/Developmental Toxicity LOAEL = 51 (F) mg/kg/day, (F1 females), based on decrease in pre-mating body-weight gain (10%) Offspring and Reproductive Toxicity NOAEL = 16 mg/kg/day (M/F) mg/kg/day Offspring and Reproductive Toxicity LOAEL F1 = 40 (M/F) mg/kg/day, based on reduced gestation day 20 fetal weights; decreased postnatal day 0, 4 and 7 pup weights; decreased pup survival; delayed vaginal patency; reduced epididymal, prostate, and testicular weights. Additional information supports the conclusions reached in the 2-gen reproduction study (MRID 43345408)
870.4100b Chronic toxicity (dog)	43345406 (1994) Acceptable/Guideline 0, 300, 800, and 1800 ppm M/F: 0, 9.9/10.4, 24.9/29.6 & 61.2/61.9 mg/kg/day	Systemic toxicity NOAEL = 24.9/29.6 mg/kg/day for males/and females Systemic toxicity LOAEL = 61.2/61.9 mg/kg/day (M/F), based upon compensated normochromic microcytosis.

Guideline No./Study Type	MRID No. (year)/Classification/ Doses	Results
870.4200 Carcinogenicity rodents (mouse)	43345407 (1994) Acceptable/Guideline 0, 300, 600, 1000, & 2000 ppm M/F: 0, 46.6/58.0, 93.9/116.9, 160.5/198.0 & 337.6/407.1 mg/kg/day	Systemic toxicity NOAEL = 93.9 mg/kg/day for males and 116.9 mg/kg/day for females Systemic toxicity LOAEL = 160.5 mg/kg/day for males and 198.0 mg/kg/day for females, based on dose-related decreases in hemoglobin and hematocrit by study termination. No evidence of carcinogenicity.
870.4300 Combined chronic toxicity/carcinogenicity rodents (rat)	43345409 (1994) Acceptable/Guideline M: 0, 600, 1000, 2000, & 3000 ppm F: 0, 300, 600, 1000 & 2000 ppm M/F: 0/0, 24.3/20, 40/36.4, 82.8/67, & 123.5/124.7 mg/kg/day	Systemic toxicity NOAEL = 40 mg/kg/day for males and 36.4 mg/kg/day for females Systemic toxicity LOAEL = 82.8 mg/kg/day for males and 67 mg/kg/day for females, based on dose-related decreased body weights (11 & 19%), body-weight gains (13 & 26%), food consumption (13 & 19%), hemoglobin, hematocrit, mean cell volume, and mean cell hemoglobin. Increased nucleated red blood cells and reticulocytes in bone of females at 124.7 mg/kg/day. No evidence of carcinogenicity.
870.5100 Gene Mutation: Ames assay Gene Mutation: HGPRT	41911611 (1986) Acceptable/Guideline Salmonella typhimurium strains TA1535, TA1538, TA1537, TA98 and TA100 were exposed to Sulfentrazone Technical (95.5%) at concentrations of 100-10,000 ug/plate with or without S9 activation (both trials).	No evidence of compound-induced cytotoxicity was evident either in presence or in absence of S9 activation. The positive controls induced the expected mutagenic responses in the appropriate tester strain. Sulfentrazone was considered not mutagenic under any test condition.
870.5300 In vitro mammalian cell gene mutation assay (mouse lymphoma)	43004604 (1992) Acceptable/Guideline Mouse lymphoma (L5178Y $TK^{+/-}$ CHO) cells were exposed to Sulfentrazone Technical (94.2%) in non-activated dose ranges of 424-1308ug/ml (Trial 1) and 1308-3000 ug/ml (Trial 2); With S9 activation dose ranges of 424-1407 ug/ml (Trial 1) and 915-1800 ug/ml (Trial 2).	In a forward gene mutation assay, sulfentrazone at precipitating levels were equivocally positive in the absence of S9 activation. This response was not repeated at doses up to 1800:g/ml in the presence of S9 activation.
870.5395 Mammalian erythrocyte micronucleus test	43004605 (1992) Acceptable/Guideline Groups of 5 male and 5 female ICR mice received single intraperitoneal injection of 85, 170, and 340 mg/kg Sulfentrazone Technical (94.2%). Test material was administered in corn oil and bone marrow cells harvested at 24, 48, and 72 hours post-dosing. Cyclophosphamide at 30 mg/kg was used as positive control.	The test was negative in mice administered single intraperitoneal doses of 85-340 mg/kg. The 340 mg/kg dose was estimated to be approximately 80% of the LD50/7. No evidence of a cytotoxic effect on the target organ and no significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow cells.

Guideline No./Study Type	MRID No. (year)/Classification/ Doses	Results
870.5450 Dominant lethal assay - rodent	44248302 (1996) Acceptable/Guideline In dominant lethal assay male rats were dosed at 0, 100, 225, or 450 mg/kg/day for 5 days, and mated to untreated females sequentially for 10 weeks to determine the level of fetal deaths due to dominant lethal mutations.	There were no significant differences from negative controls in the proportion of early dead: total implants, and (total) dead: total implants. Based on the results, sulfentrazone is considered negative for inducing dominant lethal mutations in pre-meiotic, meiotic, and post-meiotic germ cells of male rats under conditions of this assay up to the estimated MTD.
870.6200a Acute Neurotoxicity Study	43345405 (1994) Acceptable/Guideline 0, 250, 750, & 2000 mg/kg/day	Systemic Toxicity NOAEL = 250 mg/kg/day Systemic Toxicity LOAEL = 750 mg/kg/day, based upon increased incidence of clinical signs, FOB findings, and decreased motor activity which was reversed by day 14 post dose. No evidence of neuropathology at any dose.
870.6300 Developmental Neurotoxicity Study (rat)	de Castro, *et al.*, (2007) Acceptable/non-guideline 0, 25, or 50 mg/kg bw/day	Offspring NOAEL not observed Offspring LOAEL = 25 mg/kg/day, based on dose-dependent, statistically significant delayed ear opening, decreased grip response and rearing frequency, and increased surface righting reflex reaction time. No effect on maternal body weight (only parameter tested) during gestation.
870.7485 Metabolism and pharmacokinetics (rat)	43345410 (1994) Acceptable/Guideline Phenyl -14C - sulfentrazone (98% pure.) was administered to Sprague-Dawley rats (5 animals/sex/dose) by gavage as a single dose at levels of 50 and 500 mg/kg, or as a single dose of 50 mg/kg following a 14-day pretreatment with non-radioactive sulfentrazone (50 mg/kg/day).	Sulfentrazone was readily absorbed and 84 to 104% of the administered dose was excreted in urine and feces within 72 hours. There were no major sex differences in the pattern of excretion. Almost all the radioactivity in the urine was 3-hydroxy-methyl-F6285 (84 - 104% of the administered dose). In the feces, HMS accounted for 1.26 to 2.55% of the administered dose. The proposed metabolic pathway appeared to be conversion of the parent compound mainly to 3-hydroxymethyl-F6285 (excreted in the urine). A small amount of 3-hydroxymethyl-F6285 was also converted to 3-carboxylic acid-F6285 (excreted in the urine and feces).

13544

R168772

Chemical Name: Sulfentrazone

PC Code: 129081
HED File Code: 14000 Risk Reviews
Memo Date: 4/7/2009
File ID: DPD362324
Accession #: 000-00-0130

HED Records Reference Center
4/16/2009