UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: February 23, 2005

Subject: Orthosulfamuron: Occupational Exposure Risk Assessment for a Crop Destruct Experimental Use Permit (EUP) for Use on Rice

PC Code: 108209
DP Barcode: 304193

Chemical Class: Herbicide
Trade Name: IR5878 50 WG
IR5878 0.5 GR

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INTRODUCTION

Isagro S.p.A. has requested a crop destruct experimental use permit (EUP) for orthosulfamuron for use in controlling weeds in rice early in the growing season. Crop destruct includes the harvesting of rice to collect yield data. Once yield data are collected, the rice will be discarded on the ground of the test plot. The remaining crops/plants will be chopped (tractor mounted thrasher mower) into mulch and burned. The test plot will then be disked under by standard disking practice. The proposed use will entail a maximum of 928 lbs of formulated product [14 lbs active ingredient (ai)] on 200 acres between March 2005 and March 2006. The application rate is 0.055-0.069 lb ai/acre (A) of IR5878 50 WG and 0.066 lb ai/A of IR5878 0.5 GR per year. This assessment will address the occupational risks resulting from the proposed EUP. Based on the number of seasonal applications indicated on the product labels and information provided by the registrant, non-dietary exposures are expected to be short-term (defined as 1-30 days) in duration.

1.0 EXECUTIVE SUMMARY

Orthosulfamuron (1-(4,6-dimethoxypyrimidin-3[2-(dimethylcarbamoyl) phenylsulfamoyl] urea) is a systemic herbicide belonging to the sulfonylurea class of chemicals. It is being proposed for control of broadleaf weeds and sedges in rice. The mode of action for orthosulfamuron is through inhibition of the plant enzyme acetolactate synthase, which is also known as acetohydroxy acid synthase. Inhibition of this enzyme blocks branch-chain amino acid biosynthesis of valine, leucine, and isoleucine involved in plant growth processes leading to death of the plant. The proposed use is for orthosulfamuron formulated from 0.51 % ai as a granule (IR5878 0.5 GR) to 51.5% ai as a water dispersible granule (IR5878 50 WG).

Hazard Characterization

The experimental use of orthosulfamuron can be supported by the toxicology data submitted by the registrant.

The acute toxicity data indicate that the IR5878 technical (98%) product and its additional formulations (IR5878 0.5 GR and IR5878 50 WG) all have low toxicity (Category IV) via oral, dermal, and inhalation (study waived for IR5878 0.5 GR) routes of exposure. IR5878 technical and IR5878 0.5 GR are both non-irritating to the skin, while IR5878 50 WG is a mild irritant, causing erythema and eschar. They are all moderate eye irritants (Category III) resulting in conjunctivitis. None are dermal sensitizers under the conditions of this study.

The database on orthosulfamuron indicates that the liver and kidney are target organs for this chemical. There is also indication that the neuromuscular system may be affected by orthosulfamuron. In a 13 week toxicity study in dogs, liver toxicity included increased absolute and relative liver weights accompanied by alterations in clinical chemistry (increased levels of alkaline phosphatase). These effects were seen at the high dose (1000 mg/kg/day) in both male and female dogs. The 13 week studies in the rat and the mouse did not demonstrate toxicity at

any dose level. A 2-generation reproduction study in rats demonstrated kidney lesions (tubular mineralization, calculi and urothelia hyperplasia) in the F_0 and F_1 females at the highest dose tested (765 and 888 mg/kg/day, respectively). In addition, a functional observation battery (FOB) revealed markedly decreased locomotor activity in the high dose F_1 males (712 mg/kg/day). Since this observation indicated a possible neurotoxic effect, a Section 3 registration for this product will need to include neurotoxicity studies. In an orthosulfamuron (IR 5878) data summary supplied by the registrant, a list of studies to be submitted for Section 3 application did not include any neurotoxicity studies.

In the prenatal toxicity studies in rabbits and rats with orthosulfamuron, there is no evidence of toxicity (maternal or developmental) at the highest doses tested (250 and 1000 mg/kg/day, respectively). A LOAEL was not determined for the prenatal developmental toxicity study in rabbits and the limit dose of 1000 mg/kg/day was not used in the study. Dose selection was based on results from a preliminary developmental toxicity study in rabbits. In the preliminary study, dose levels ≥250 mg/kg bw/day exhibited maternal toxicity, indicated by decreased body weight gains, decreased food consumption and abortion. At dose levels ≥500 mg/kg bw/day, clinical signs included conjunctival redness, maternal deaths, resorptions, and fetal malformations. Based on the results of the preliminary study, the use of 250 mg/kg/day as the high-dose group in the main study is considered acceptable. Results from the developmental and reproductive toxicity studies did not show increased quantitative or qualitative susceptibility as a result of *in utero* exposure to orthosulfamuron. There is no evidence that orthosulfamuron induces any endocrine disruption.

In addition, there were four mutagenicity studies submitted for orthosulfamuron. The submitted studies are acceptable and satisfy the mutagenicity test battery. All studies tested negatively under the conditions of the assays. For risk characterization purposes, a dermal and inhalation absorption factor of 100% was used. The toxicity profiles for orthosulfamuron are located in the appendix.

For short-term occupational risk assessment, the NOAEL of 165 mg/kg/day from the 2-generation reproductive study was chosen for both dermal and inhalation exposures. Decreased locomotor activity was observed in F_1 males at the LOAEL of 712 mg/kg/day.

Occupational Exposure (agricultural and commercial)

The following agricultural products have been assessed for occupational exposure: IR5878 50 WG and IR5878 0.5 GR.

IR5878 50 WG contains 51.5% orthosulfamuron in a water-dispersible granular formulation for use as an agricultural herbicide on rice. The proposed application rate is 0.055-0.069 lbs ai/A applied by groundboom and aerial equipment. IR5878 50 WG Herbicide will be applied 1 time per year early in the growing season (2-4 leaves), at a maximum application rate of 0.069 lbs ai/A/season. Based on the number of seasonal applications indicated on these product labels, and information provided by the registrant, handler exposures are expected to be short-term in duration.

IR5878 0.5 GR contains 0.51% orthosulfamuron in a granular formulation for use as an agricultural herbicide on permanently flooded rice. The proposed application rate is 0.066 lbs ai/A applied by ground (tractor drawn spreader) and aerial equipment. IR5878 0.5 GR Herbicide will be applied 1 time per year early in the growing season (1-2 leaves), at a maximum application rate of 0.066 lbs ai/A/season. Based on the number of seasonal applications indicated on these product labels, and information provided by the registrant, handler exposures are expected to be short-term in duration.

Handlers

No chemical-specific data for assessing handler exposures were submitted to the Agency in support of the proposed uses; therefore, HED used surrogate data from the Pesticide Handlers Exposure Data Base (PHED) Version 1.1, and standard values established by the Health Effects Division (HED) Science Advisory Council for Exposure were used for acres treated per day, body weight and the level of personal protective equipment worn by handlers. The handler exposure estimates in this assessment are based on a central tendency estimate of unit exposure (from PHED) and an upper-percentile assumption for the application rate, and they are considered to be representative of high-end exposures. The estimated exposures are believed to be reasonable high-end estimates based on observations from field studies and professional judgement.

Since both the dermal and inhalation endpoints were the same for short-term duration, the route specific MOEs were combined and compared to the NOAEL. The total MOEs for short-term handlers range from 11,000 to 260,000 and do not exceed HED's level of concern (MOEs < 100).

Postapplication

No postapplication data were submitted in support of this registration action. Based on the number of seasonal applications indicated on the proposed product labels and information provided by the registrant, no postapplication exposures are expected. Since the products (IR5878 50 WG and IR5878 0.5 GR) are herbicides used early in the growing season, postapplication exposure is expected to be minimal and less than the application exposure. Based on this information, a postapplication exposure assessment was neither required, nor performed.

Recommendation

HED has no objections to the requested EUP on rice. However, HED advises that the labels clearly state the application rates in weights of both product and active ingredient per acre.

2.0 HAZARD CHARACTERIZATION

2.1 Hazard Profile

The toxicological endpoints for short- and intermediate-term dermal and inhalation exposure were chosen from the 2-generation reproduction study in rats (MRID 46219033) and are summarized in Table 2.

Short-term dermal and inhalation exposure was based on a decrease in locomotor activity in F_1 males. The LOAEL is 712 mg/kg/day and the NOAEL is 165 mg/kg/day. At 6 weeks of age, the parental F_1 animals were subjected to a Functional Observational Battery (FOB) and tested for motor activity. Compared to control males, high dose males (712 mg/kg/day) had a 76% decrease in locomotor activity at all time points. Based on the severity of the effect seen, it is possible that a decrease in locomotor activity could have been observed before the 6 week FOB (short-term exposure period of 1-30 days). Therefore, the selected endpoint for short-term dermal and inhalation exposure is reasonable and considered protective.

For intermediate-term dermal and inhalation exposure the LOAEL is 712 mg/kg/day and was based on a decrease in locomotor activity in F_1 males and kidney lesions in F_0 and F_1 females. The NOAEL is 165 mg/kg/day.

Since there were no dermal or inhalation studies submitted for orthosulfamuron, dermal and inhalation endpoints were based on an oral reproduction study. A dermal and inhalation absorption factor of 100% was used to calculate margins of exposure (MOEs). Furthermore, since both the dermal and inhalation endpoints were based on the same toxicological effects, the MOEs were combined into a total MOE. The target MOE for both dermal and inhalation exposure is 100.

Table 2. Summary of Toxicological Doses and Endpoints for Orthosulfamuron

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (females 13-49)	N/A	N/A	No risk assessment is required
Acute Dietary (general population)	N/A	N/A	No risk assessment is required
Chronic Dietary (all populations)	N/A	N/A	No risk assessment is required
Incidental Oral Short-Term (1 - 30 days)	N/A	N/A	No risk assessment is required
Incidental Oral Intermediate-Term (1 - 6 months)	N/A	N/A	No risk assessment is required
Dermal	NOAEL (mg/kg/day):	Occupational LOC for	2-generation reproduction study

Table 2. Summary of Toxicological Doses and Endpoints for Orthosulfamuron			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Short-Term (1 - 30 days)	165	MOE = 100	LOAEL 712 (mg/kg/day): based on decreased locomotor activity in F_1 males
Dermal Intermediate-Term (1 - 6 months)	NOAEL (mg/kg/day): 165	Occupational LOC for MOE = 100	2-generation reproduction study LOAEL 712 (mg/kg/day): based on decreased locomotor activity in F_1 males and kidney lesions in F_0 and F_1 females
Inhalation Short-Term (1 - 30 days)	NOAEL (mg/kg/day): 165	Occupational LOC for MOE = 100	2-generation reproduction study LOAEL 712 (mg/kg/day): based on decreased locomotor activity in F_1 males
Inhalation Intermediate-Term (1 - 6 months)	NOAEL (mg/kg/day): 165	Occupational LOC for MOE = 100	2-generation reproduction study LOAEL 712 (mg/kg/day): based on decreased locomotor activity in F_1 males and kidney lesions in F_0 and F_1 females
Cancer (oral, dermal, inhalation)	**Classification:** A cancer risk assessment is not required for experimental use permits		

3.0 PROPOSED END-USE PRODUCTS/PATTERNS

Table 3 summarizes the proposed use pattern and formulation specified in the two end-use products containing orthosulfamuron.

TABLE 3: PROPOSED USE PATTERNS AND FORMULATIONS				
Formulation	**Method of Application**	**Use Sites**	**Application Rates**	**Timing of Application**
IR5878 50 WG Herbicide - water-dispersible granule (51.5 % ai)	ground and aerial spray	rice	0.055 - 0.069 lbs ai/A	1 app/season; Max seasonal rate = 0.069 lbs ai/A; Apply to young emerging and actively growing weeds, between 2-4 leaves. Lowest application rate is intended for use with other compounds.
IR5878 0.5 GR Herbicide - granular (0.51 % ai)	ground and aerial spray	rice	0.066 lbs ai/A	1 app/season; Max seasonal rate = 0.066 lbs ai/A; Apply to young emerging weeds, between 1-2 leaves. Apply to permanently flooded rice only.

4.0 NON-OCCUPATIONAL/RESIDENTIAL EXPOSURE

Since orthosulfamuron is a new active ingredient (ai), there are no registered residential uses associated with orthosulfamuron. Therefore, a quantitative non-occupational exposure assessment was not performed.

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 employed for orthosulfamuron. 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 data base 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.

5.0 OCCUPATIONAL EXPOSURE

5.1 Handlers

The following agricultural products have been assessed for occupational exposure: IR5878 50 WG and IR5878 0.5 GR.

IR5878 50 WG contains 51.5% orthosulfamuron in a water-dispersible granular formulation for use as an agricultural herbicide on rice. The proposed application rate is 0.055 - 0.069 lbs ai/A applied by groundboom and aerial equipment. IR5878 50 WG Herbicide will be applied 1 time per year early in the growing season (2-4 leaves), at a maximum application rate of 0.069 lbs ai/A/season. Based on the number of seasonal applications indicated on these product labels, and information provided by the registrant, handler exposures are expected to be short-term in duration.

IR5878 0.5 GR contains 0.51% orthosulfamuron in a granular formulation for use as an agricultural herbicide on permanently flooded rice. The proposed application rate is 0.066 lbs ai/A applied by ground (tractor drawn spreader) and aerial equipment. IR5878 50 WG Herbicide will be applied 1 time per year early in the growing season (1-2 leaves), at a maximum application rate of 0.066 lbs ai/A/season. Based on the number of seasonal applications indicated on these product labels, and information provided by the registrant, handler exposures are expected to be short-term in duration.

Based on the information provided by the registrant, handler exposures are expected to be short-term in duration. The following exposure scenarios have been assessed:

- Loading Granular Formulation for Tractor Drawn Spreader
- Loading Granular Formulation for Aerial Fixed Wing
- Mixing/Loading Dry Flowable (Water-Dispersible Granule) Formulation for Groundboom
- Mixing/Loading Dry Flowable (Water-Dispersible Granule) Formulation for Aerial Fixed Wing
- Applying Sprays using Groundboom
- Applying Sprays using Aerial Fixed Wing
- Applying Granules using Aerial Fixed Wing
- Applying Granules with Tractor Drawn Spreader
- Flagging Sprays
- Flagging Granules

5.1.1 Data and Assumptions for Handler Exposure Scenarios

The following assumptions, parameters and factors were used in this risk and exposure assessment:

- Non-cancer application rates were based on the maximum rates on the proposed labels.

- Unit Exposures:

  - Chemical-specific data for assessing exposure during pesticide handling activities were not submitted to the Agency in support of this Section 3 application. It is HED policy to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific data are not available (HED Science Advisory Council for Exposure, SOP Number 7, January 1999).

  - Occupational handler exposure assessments were completed by HED using baseline level of Personal Protective Equipment (PPE). The baseline clothing level for occupational exposure scenarios is generally an individual wearing long pants, a long-sleeved shirt, no chemical-resistant gloves, and no respirator.

- A dermal absorption factor of 100 % was used to calculate non-cancer risks.

- Area Treated:

  - Based on information provided by the registrant, the following ***acres per day treated*** were assumed:

  - 200 acres/day for mixing/loading and applying dry flowable (water-dispersible granule) to rice using aerial equipment
  - 200 acres/day for mixing/loading and applying dry flowable (water-dispersible granule) to rice using groundboom
  - 200 acres/day for loading and applying granular to rice using aerial equipment
  - 200 acres/day for loading and applying granular to rice using tractor drawn spreader

- 200 acres/day for flagging liquids to rice using aerial equipment
- 200 acres/day for flagging granules to rice using aerial equipment

- Body Weight:

  - A female body weight of 60 kg was used for short-term exposure assessments based on effects (kidney lesions) seen in the 2-generation reproduction study in the rat.

Equations/Calculations:

The following equations were used to calculate handler exposure and risk:

$$\textit{Dermal Dose (mg/kg/day)} = \frac{\textit{Rate (lb ai/A) x UE (mg/lb ai) x DA x Acres Treated (A/day)}}{\textit{BW (kg)}}$$

$$\textit{Inhalation Dose (mg/kg/day)} = \frac{\textit{Rate (lb ai/A) x UE (mg/lb ai) x Acres Treated (A/day)}}{\textit{BW (kg)}}$$

Where:

Rate (Application Rate)	=	Maximum application rate on product label (lb ai/A)
UE (Unit Exposure)	=	Exposure value derived from August 1998 PHED Surrogate Exposure Table
DA (dermal absorption factor)	=	Factor to account for dermal absorption when endpoint is selected from a 2-generation reproduction study (100 %)
Acres Treated	=	Maximum number of acres treated per day (200 A/day) derived from information provided by the registrant
BW	=	Body weight (60 kg)

$$\textbf{Short-term Dermal MOE} = \frac{\textbf{NOAEL (165 mg/kg/day)}}{\textbf{Dermal Dose (mg/kg/day)}}$$

$$\textbf{Short-term Inhalation MOE} = \frac{\textbf{NOAEL (165 mg/kg/day)}}{\textbf{Inhalation Dose (mg/kg/day)}}$$

$$\textit{Total Dose (mg/kg/day)} = \textit{Dermal Dose (mg/kg/day)} + \textit{Inhalation Dose (mg/kg/day)}$$

$$\textit{Total MOE} = \textit{Short-term NOAEL (165 mg/kg/day)/Total Dose (mg/kg/day)}$$

5.1.2 Exposure and Risk

Summaries of the non-cancer (MOEs) short-term risks for handlers at the baseline are included in **Table 4.** Since both the dermal and inhalation endpoints were the same for short-term duration, the route specific MOEs were combined and compared to the NOAEL. The total MOEs for short-term handlers range from 11,000 to 260,000 and do not exceed HED's level of concern (MOEs < 100).

The handler exposure estimates in this assessment are based on a central tendency estimate of unit exposure and an upper-percentile assumption for the application rate and are assumed to be representative of high-end exposures. The uncertainties associated with this assessment stem from the use of surrogate exposure data (e.g., differences in use scenario and data confidence) and assumptions regarding the amount of chemical handled. The estimated exposures are believed to be reasonable high-end estimates based on observations from field studies and professional judgement. It should be noted that the unit exposures are the same with or without gloves for the following scenarios: dry flowable mixing/loading for aerial and groundboom (3,4), groundboom application (7), and aerial application for granular formulation (6). However, the data confidence is higher with gloves. Based on professional judgement, gloves are recommended.

5.2 Postapplication

No postapplication data were submitted in support of this registration action. Based on the number of seasonal applications indicated on the proposed product labels and information provided by the registrant, no postapplication exposures are expected. As specified by the registrant (James Messina, email dated 2/16/05), the application of IR5878 occurs early in the rice growing life (2-4 leafstage of rice). Rice is typically planted in April/May and IR5878 is applied shortly after the rice starts growing (approximately 2-3 weeks after planting). The rice is typically harvested in September/October and the estimated timeframe between application and harvest is approximately 3-4 months. Since the products (IR5878 50 WG and IR5878 0.5 GR) are herbicides used early in the growing season, postapplication exposure is expected to be minimal and less than the application exposure. Based on this information, a postapplication exposure assessment was neither required, nor performed.

Table 4: Short-term Handler Exposure and Risk for Orthosulfamuron											
Exposure Scenario #	**Mitigation Level**	**Dermal Unit Exposure (mg/lb ai)**	**Inhalation Unit Exposure (µg/lb ai)**	**Application Rate**	**Amount Treated**	**Dermal Dose (mg/kg/day) [a]**	**Inhalation Dose [b] (mg/kg/day)**	**Dermal MOE [c]**	**Inhalation MOE [d]**	**Total Dose [e]**	**Total MOE [f]**
Mixer/Loader & Loader											
Granular for Aerial Application (1)	Baseline	0.0084	1.7 (0.0017 mg/lb ai)	0.066 lb ai/A	200 Acres/day	0.00185	0.00037	89,000	450,000	0.0022	75,000
Granular for Solid Broadcast Spreader Application (2)	Baseline	0.0084	1.7 (0.0017 mg/lb ai)	0.066 lb ai/A	200 Acres/day	0.00185	0.00037	89,000	450,000	0.0022	75,000
Dry Flowable (water-dispersible granule) for Aerial Application (3)	Baseline	0.066	0.77 (0.00077 mg/lb ai)	0.055 lb ai/A	200 Acres/day	0.0121	0.00014	14,000	1,200,000	0.0122	14,000
				0.069 lb ai/A		0.0152	0.00018	11,000	920,000	0.0154	11,000
Dry Flowable (water-dispersible granule) for Groundboom Application (4)	Baseline	0.066	0.77 (0.00077 mg/lb ai)	0.055 lb ai/A	200 Acres/day	0.0121	0.00014	14,000	1,200,000	0.0122	14,000
				0.069 lb ai/A		0.0152	0.00018	11,000	920,000	0.0154	11,000
Applicator											
Sprays for Aerial Application (5)	Engineering Control	0.005	0.068 (0.000068 mg/lb ai)	0.055 lb ai/A	200 Acres/day	0.00092	0.000012	180,000	14,000,000	0.00093	180,000
				0.069 lb ai/A		0.0012	0.000015	140,000	11,000,000	0.00122	140,000
Aerial Application (granular formulation) (6)	Baseline	0.0017	1.3 (0.0013 mg/lb ai)	0.066 lb ai/A	200 Acres/day	0.00037	0.00029	450,000	570,000	0.00066	250,000
Sprays for Groundboom Application (7)	Baseline (open cab)	0.014	0.74 (0.00074 mg/lb ai)	0.055 lb ai/A	200 Acres/day	0.0026	0.00014	63,000	1,200,000	0.0027	61,000
				0.069 lb ai/A		0.0032	0.00017	52,000	970,000	0.0034	49,000
Solid Broadcast	Baseline	0.0099	1.2	0.066 lb ai/A	200	0.0022	0.00026	75,000	630,000	0.0025	66,000

Table 4: Short-term Handler Exposure and Risk for Orthosulfamuron											
Exposure Scenario #	**Mitigation Level**	**Dermal Unit Exposure (mg/lb ai)**	**Inhalation Unit Exposure (µg/lb ai)**	**Application Rate**	**Amount Treated**	**Dermal Dose (mg/kg/day) [a]**	**Inhalation Dose [b] (mg/kg/day)**	**Dermal MOE [c]**	**Inhalation MOE [d]**	**Total Dose [e]**	**Total MOE [f]**
Spreader Application (8)	(open cab)		(0.0012 mg/lb ai)		Acres/day						
Flagger											
Liquid for Aerial Application (liquid formulation) (9)	Baseline	0.011	0.35 (0.00035 mg/lb ai)	0.055 lb ai/A	200 Acres/day	0.0020	0.000064	83,000	2,600,000	0.0021	79,000
				0.069 lb ai/A		0.0025	0.000080	66,000	2,100,000	0.0026	63,000
Aerial application (granular formulation)(10)	Baseline	0.00275 [g]	0.15 (0.00015 mg/lb ai)	0.066 lb ai/A	200 Acres/day	0.00061	0.000033	270,000	5,000,000	0.00064	260,000

a. Short-term Dermal Dose (mg/kg/day) = Rate (lb ai/A) x UE (mg /lb ai) x DA (100 %) x Acres Treated (A/day) / BW (60 kg)

b. Short-term Inhalation Dose (mg/kg/day) = Rate (lb ai/A) x UE (mg /lb ai) x Acres Treated (A/day) / BW (60 kg)

c. Short-term Dermal MOE = Dermal NOAEL (165 mg/kg/day) / Dermal Dose (mg/kg/day)

d. Short-term Inhalation MOE = Inhalation NOAEL (165 mg/kg/day) / Inhalation Dose (mg/kg/day)

e. Total Dose (mg/kg/day) = Dermal Dose + Inhalation Dose

f. Total MOE = Short-term NOAEL (165 mg/kg/day)/ Total Dose

g. Dermal Unit Exposure = 0.00458x0.5+0.0004619=0.00275

APPENDIX A

Table 1a. Acute Toxicity Profile - Orthosulfamuron Technical (98.0 % Orthosulfamuron, 2.0% Inert Ingredients)				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute oral-rat	46219019	LD_{50} = >5000 mg/kg/bw (both sexes)	IV
870.1200	Acute dermal-rat	46219020	LD_{50} = >5000 mg/kg/bw (both sexes)	IV
870.1300	Acute inhalation-rat	46219021	LC_{50} = >2.19 mg/L (both sexes)	IV
870.2400	Acute eye irritation-rabbit	46219022	conjunctivitis, moderate irritant	III
870.2500	Acute dermal irritation -rabbit	46219023	non-irritant	IV
870.2600	Skin sensitization-guinea pig	46219024	Not a sensitizer	N/A

Table 1b. Acute Toxicity Profile - Orthosulfamuron (0.5 % Orthosulfamuron, 99.5% Inert Ingredients)				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute oral-rat	46219052	LD_{50} = >5000 mg/kg/bw (both sexes)	IV
870.1200	Acute dermal-rat	46219053	LD_{50} = >5000 mg/kg/bw (both sexes)	IV

870.1300	Acute inhalation-rat	N/A	study was waived large product granules (100-300 x greater than 10 microns), unlikely to be deposited into lungs	N/A
870.2400	Acute eye irritation-rabbit	46219054	conjunctivitis, moderate irritant	III
870.2500	Acute dermal irritation -rabbit	46219055	non-irritant	IV
870.2600	Skin sensitization-guinea pig	46219056	Not a sensitizer	N/A

Table 1c. Acute Toxicity Profile - Orthosulfamuron (51.5 % Orthosulfamuron, 48.5 % Inert Ingredients)				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute oral-rat	46219062	LD_{50} = >5000 mg/kg/bw (both sexes)	IV
870.1200	Acute dermal-rat	46219064	LD_{50} = >5000 mg/kg/bw (both sexes)	IV
870.1300	Acute inhalation-rat	46219066	LC_{50} = >4.38 mg/L (both sexes)	IV
870.2400	Acute eye irritation-rabbit	46219068	conjunctivitis, moderate irritant	III
870.2500	Acute dermal irritation -rabbit	46219070	erythema/eschar mild-irritant	IV
870.2600	Skin sensitization-guinea pig	46219072	Not a sensitizer	N/A

Table 2. Subchronic, Chronic and Other Toxicity Profile-Orthosulfamuron				
GDLN	**Study Type**	**Dose Levels**	**MRID**	**Results**
870.3100	2001-13 WEEK FEEDING-RAT	ppm= 0, 250, 1500, 9000 mg/kg/day= M: 0, 19, 113, 706 F: 0, 22, 131, 773	46260103	NOAEL (mg/kg/day): 706 LOAEL (mg/kg/day): not determined
870.3100	2001-13 WEEK FEEDING-MOUSE	ppm= 0, 250, 1250, 6000 mg/kg/day= M: 0, 36, 187, 865 F: 0, 47, 228, 1096	46260102	NOAEL (mg/kg/day): 865 LOAEL (mg/kg/day): not determined
870.3100	2001-13 WEEK FEEDING-DOG	mg/kg/day= 0, 150, 450, 1000	46219027	NOAEL (mg/kg/day): 450 LOAEL (mg/kg/day): 1000 based on increased alkaline phosphatase levels, increased absolute and relative liver weights
870.3700	2001-DEVELOPMENTAL TOXICITY-RAT	mg/kg/day= 0, 100, 300, 1000	46219031	Maternal: NOAEL (mg/kg/day): 1000 LOAEL (mg/kg/day): not determined Developmental: NOAEL (mg/kg/day): 1000 LOAEL (mg/kg/day): not determined

Table 2. Subchronic, Chronic and Other Toxicity Profile-Orthosulfamuron				
GDLN	**Study Type**	**Dose Levels**	**MRID**	**Results**
870.3700	2001-DEVELOPMENTAL TOXICITY-RABBIT	mg/kg/day= 0, 25, 75, 250	46219029	Maternal: NOAEL (mg/kg/day): 250 LOAEL (mg/kg/day): not determined Developmental: NOAEL (mg/kg/day): 250 LOAEL (mg/kg/day): not determined
870.3800	2003-2-GENERATION REPRODUCTION-RAT	ppm=(males/females) 0, 350/225, 1400/900, 5600/3600 mg/kg/day= F_0M: 0, 38, 145, 635 F_0F: 0, 48, 205, 765 F_1M: 0, 41, 165, 712 F_1F: 0, 53, 215, 888	46219033	Parental: NOAEL (mg/kg/day): M=145-165, F= 205-215 LOAEL (mg/kg/day): M=635-712, F= 765-888 based on decreased locomotor activity in F_1 males and kidney lesions in F_0 and F_1 females Reproductive: NOAEL (mg/kg/day): M=635-712, F= 765-888 LOAEL (mg/kg/day): not determined Offspring: NOAEL (mg/kg/day): M=635-712, F= 765-888 LOAEL (mg/kg/day): not determined
870.5100	BACTERIAL REVERSE MUTATION ASSAY		46219034	Negative
870.5300	*IN VITRO* MAMMALIAN CELL GENE MUTATION TEST		46219036	Negative
870.5375	*IN VITRO* CHROMOSOME ABERRATION TEST		46219035	Negative
870.5395	MAMMALIAN ERYTHROCYTE MICRONUCLEUS TEST		46219037	Negative