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OFFICE OF
PREVENTION, PESTICIDES AND
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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

DATE: 7/18/02

SUBJECT: PP#: 0F06120. **Chlorsulfuron in/on Pasture Grasses. Health Effects Division (HED) Risk Assessment.** PC Code: 118601. DP Barcode: D266070. Case #: 292904. Submission #: S613409

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration Division (RD) of OPP has requested that HED estimate the risk to human health that will result from the proposed uses of chlorsulfuron, 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino] carbonyl]benzenesulfonamide in/on grass (pasture and rangeland). HED evaluated hazard and exposure data and conducted dietary, occupational, residential and aggregate exposure assessments.

A summary of the findings and an assessment of human risk resulting from the proposed uses of chlorsulfuron is provided in this document. The risk assessment, the residue chemistry data review, and the dietary risk assessment were provided by Felecia Fort (RRB1), the hazard characterization by Linda Taylor (RRB1), the occupational/residential exposure assessment by Susan Hanley (RRB1), and the drinking water assessment by Lucy Shanaman of the Environmental Fate and Effects Division (EFED).

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1.0 EXECUTIVE SUMMARY

Chlorsulfuron is a selective herbicide currently registered for use on barley, oats, wheat, fallow fields and ornamental turf to control grasses and broadleaf weeds. The petitioner, E. I. DuPont de Nemours and Company is proposing a new use on pasture and rangeland grasses. In conjunction with this registration, the petitioner is requesting and HED is recommending for the establishment of the following permanent tolerances for residues of chlorsulfuron 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino] carbonyl]benzenesulfonamide:

Grasses, forage	0.01 ppm
Grasses, hay	0.01 ppm

This risk assessment incorporates several worst case assumptions and is considered to be a very conservative estimate of risk to chlorsulfuron. Several deficiencies are noted in the toxicity database; however, the available data base provide enough information for selection of toxicity endpoint and doses for estimating risk. Based on the available data and estimated risk, HED has no objections to the establishment of a conditional registration and permanent tolerances for residues of chlorsulfuron in/on pasture and rangeland grasses. Human health risks are considered to be minimal due to its low acute toxicity (acute categories III and IV), low dietary and occupational/residential risk, and its "no evidence of carcinogenicity" classification.

Chlorsulfuron is a member of the sulfonylurea class of pesticides that include primisulfuron, chlorimuron-ethyl and metsulfuron-methyl. In general, the mode of action for the sulfonylureas is by entering the plant through the root and inhibiting the synthesis of amino acids. It is applied via groundboom sprayer, handheld sprayers and aerial application. Chlorsulfuron is the active ingredient in DuPont Telar and Glean Herbicides which have been registered in the United States since the early 1980's. Chlorsulfuron is currently under re-registration on List A. The Registration Standard was completed 9/82. A Registration Standard Update was issued 2/20/91.

Hazard Assessment

Chlorsulfuron has low acute toxicity via the oral, dermal, and inhalation routes. Adequate data are not available for an assessment of eye or skin irritation potential or for dermal sensitization potential. A 21-day repeat dose dermal study and a subchronic inhalation study are also not available for chlorsulfuron.

The chronic data provide no evidence that chlorsulfuron is particularly toxic to any organ or tissue. Neurotoxicity was not observed in any study on chlorsulfuron.

Developmental toxicity was observed in both the rat and rabbit, as evidenced by decreased fetal body weights in both species. Maternal toxicity was observed as decreased body-weight gain in the rabbit and as an increased incidence of clinical signs [vaginal discharge with alopecia] in the rat.

Reproductive toxicity was observed in the rat, as evidenced by a slight decrease in maternal fertility in the F3 generation [both litters]. No parental or offspring toxicity was observed. Although this study conformed to the old guideline requirements, it is unacceptable under the current guideline requirements in light of the fact that most of the parameters used for assessing susceptibility are not provided in the available study.

The data provided no indication of increased susceptibility [qualitative and quantitative] following *in utero* exposure to chlorsulfuron in either the rat or rabbit developmental toxicity study. Susceptibility cannot be assessed in the 3-generation reproduction study in rats. The HED HIARC determined that a 2-generation reproduction study is required for chlorsulfuron.

No effects were observed on the endocrine system in any of the available studies on chlorsulfuron.

There is also no evidence of carcinogenicity in rats or mice following oral exposure to chlorsulfuron. The available mutagenic data indicate chlorsulfuron is not mutagenic.

Chlorsulfuron is rapidly absorbed, metabolized, and eliminated in rats following oral administration. There are no remarkable sex- ,dose-, or treatment-regiment-related differences in the absorption, distribution, and excretion of chlorsulfuron in rats. The major routes of elimination are *via* the urine (58-72% of the dose) and feces (20-35%). Negligible amounts (<0.08%) of radioactivity are found in the expired air as carbon dioxide. Small amounts of radioactivity were found in the tissues 3 days after dosing, with the highest concentrations being observed in the liver and whole blood in both sexes.

Dose Response Assessment

The HED HIARC met on May 29, 2002 and again on July 11, 2002 to select toxicity endpoints for risk assessment and to evaluate the potential for increased susceptibility of infants and children from exposure to chlorsulfuron. No appropriate toxicity endpoint was available to quantitate risk from a single-dose administration of chlorsulfuron. Consequently, there is no acute reference dose (aRfD). The short- and intermediate-term incidental oral endpoints as well as the short- and intermediate term dermal and inhalation endpoints are based upon decreases in maternal body weight and body weight gain seen in a rabbit developmental toxicity study. The chronic endpoints for all routes of exposure are based upon decreased body weight observed in male rats in a chronic/carcinogenicity study. Chlorsulfuron is classified as "not likely to be carcinogenic to humans" based upon lack of evidence of carcinogenicity in rats and mice. Therefore, a cancer risk assessment is not required. Generally, when oral studies are selected as a basis for dermal endpoints, as was the case for chlorsulfuron, an absorption factor is used. Since no dermal absorption data are available, toxicity by the dermal route was considered to be equivalent to toxicity by the oral route of exposure, a default value of 100% dermal-absorption (relative to oral absorption) was used.

FQPA Decision

The Food Quality Protection Act (FQPA) required the Agency to consider potential special sensitivity to infants and children from exposure to chlorsulfuron. The FQPA Safety Factor Committee (SFC) met on June 17, 2002 and again on July 12, 2002 (electronically) to evaluate the hazard and exposure data for chlorsulfuron and recommended that the FQPA safety factor be removed (1x) in assessing the potential risk posed by this chemical. The toxicology database for chlorsulfuron contains acceptable guideline developmental studies which show no quantitative or qualitative evidence of increased susceptibility following *in utero* exposure. The HIARC concluded that there are no residual uncertainties for prenatal toxicity in the acceptable guideline developmental studies with chlorsulfuron. Although susceptibility could not be assessed in the unacceptable reproduction study, this uncertainty was accounted for by the application of a FQPA database uncertainty factor of 3X. Exposure estimates are upper bound and will not underestimate exposure to chlorsulfuron. The FQPA SFC in accordance with HIARC recommendations determined that the 3X FQPA database uncertainty factor to address data deficiencies be applied to all dietary and non-dietary residential exposure scenarios and that no Special FQPA safety factor is required. The chronic RfD and the toxicity endpoints established are considered protective of pre- and postnatal toxicity.

Based on the above mentioned endpoints, HED has selected reference doses (RfDs) for chronic exposure for dietary risk assessments and calculated Population Adjusted Doses (PADs) which are the RfDs divided by the FQPA safety factors. Since the FQPA safety factor has been removed, the PAD is equal to the RfD (0.02 mg/kg bw/day). The RfD of 0.02 mg/kg/day includes the 3X FQPA database uncertainty factor. The short-term dermal and inhalation endpoint as well as the short- and intermediate- term incidental oral endpoint chosen by HED's HIARC was decreased body weight gain seen at the oral LOAEL of 200 mg/kg/day from a developmental toxicity study in rabbits. The NOAEL for this study was 75 mg/kg/day. The standard uncertainty factors for the inter- (10X) and intra-species (10X) differences were selected for short and intermediate term exposures. The additional 3X FQPA database uncertainty factor was applied to residential scenarios. The resulting target Margin of exposure (MOE) for all residential exposure estimates is 300 while that for occupational is 100.

Dietary Exposure Estimates

A chronic dietary exposure analysis was conducted using the Dietary Exposure Evaluation Model (DEEM™, ver 7.76), which utilizes consumption data from the USDA 1989-92 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII). Acute and cancer dietary exposure analyses were not conducted since no acute doses or endpoints were selected and since chlorsulfuron was determined to be non-carcinogenic. Results of the dietary analyses showed exposure to chlorsulfuron consumed no more than 8% of the chronic PAD when using conservative assumptions of tolerance level residues and 100% crop treated. The highest exposed population subgroup was children 1 to 6 years old.

Residential Exposure Estimates

Since labels state lawn use, residential exposure risk was evaluated for adult handler and adult and toddler postapplication exposure to treated turf. The directions indicate use as a turf spot treatment with "a rate of 1.0 to 5.33 ounces per acre to cover 725 to 4000 sq.ft depending upon weed species." Due to this language, and 75 percent active ingredient concentration, 0.25 lb ai/ Acre (A) or 0.0057 lb ai/1000 sq ft. was assessed for residential spot treatment. Residential exposure risk was assessed using the Residential Exposure Assessment Standard Operating Procedures (ResSOPs) standard values and assumptions. Adult handler exposure risk was not of concern with MOEs ranging between 8800 and 190000. Postapplication exposure risks for adults and toddlers also exceeded target MOEs, ranging between 770 and 400,000. Since the ResSOPs ranged between median and high end assessments, and the use assessed was for spot treatment, not the entire lawn, the residential postapplication exposure risk assessment was conservative.

Drinking Water

The EFED provided the drinking water assessment using simulation models to estimate the potential concentration of chlorsulfuron in surface water. No drinking water monitoring data are available for chlorsulfuron A very conservative estimate of surface water Estimated Exposure Concentrations (EECs) which included all possible degradation products and a conservative estimate of degradate mobility equal to that of the parent compound, chlorsulfuron, was made. The modeling results from FIRST, using these assumed parameters, estimates pre-treatment surface water concentrations of total chlorsulfuron residues (both parent and degradation products), at an acute (peak) value of 59.7 ug/L (ppb), and a chronic (average annual) value of 41.3 ug/L (ppb).

Aggregate Assessment

In examining aggregate exposure, the Agency takes into account the available and reliable information concerning exposures from pesticide residues in food and other exposures including drinking water and non-occupational exposures, e.g., exposure to pesticides used in and around the home (residential). Risk assessments for aggregate exposure consider short-, intermediate- and long term (chronic) exposure scenarios considering the toxic effects which would likely be associated with each exposure duration. There are residential uses of chlorsulfuron; therefore, the considerations for aggregate exposure are those from food, water, and residential uses. Since conservative modeling was done to estimate concentrations in drinking water, Drinking Water Levels of Comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper concentration limit for a pesticide in drinking water based on how much of the PAD remains once exposures in food and in the home have been estimated and subtracted. For chlorsulfuron, only chronic and short- and intermediate- term DWLOCs were calculated since an acute endpoint was not selected, and chlorsulfuron is not carcinogenic.

Upon comparison of the chronic DWLOCs with the EEC for chlorsulfuron, surface water concentrations were less than the DWLOCs for all populations. Consequently, there is no chronic concern for drinking water from surface water sources.

Surface water EECs are also below the short- and intermediate term DWLOCs for chlorsulfuron. Therefore, there is no short- or intermediate- term exposure concern for drinking water from surface water sources.

Occupational Exposure Estimates

The worker exposure and risk assessment was based on the Pesticide Handler Exposure Database Version 1.1 (PHED, 1998) and standard assumptions for worker exposure. There were no chemical-specific data available to assess potential exposure to workers for chlorsulfuron. The exposure assessment used the maximum application rate range on cereal grains and pastures/lawns of 1 to 4 oz ai /acre and baseline clothing (long pants, long-sleeved shirt, socks and shoes). The acreage used were standard values for daily acreage treated in agriculture from HED Exposure Science Advisory Committee (Expo SAC) Policy #09.1. All route specific and combined MOEs are greater than the target MOE of 100 and therefore risks are not of concern (MOEs range between 1,000 and 56,000).

Due to the early season use and crops/areas with little worker activity, no postapplication exposure is expected.

Exposure Scenarios and Risk Conclusions

For the proposed uses on pasture and rangeland grass, human health risk assessments have been conducted for the following exposure scenarios: chronic dietary exposure (food only), aggregate chronic exposure (food and water), and short- and intermediate-term residential and occupational exposure, and short- term aggregate exposure. Other scenarios were not evaluated for chlorsulfuron since no acute doses or endpoints were selected for any population, it has been classified as being non-carcinogenic, and long-term residential and occupational exposure is not expected. All exposure estimates are below HED's level of concern.

Although this human health assessment is based on several conservative assumptions, several areas of the risk assessment can be refined with more data. There are several data gaps: (1) 2-generation reproduction study in the rat; (2) 21-day repeated dose dermal toxicity study; (3) subchronic inhalation study in the rat; (4) adequate mutagenicity studies [available studies can be upgraded]; (5) primary eye and skin irritation studies; and (6) dermal sensitization study. The dietary assessment could also be refined if monitoring data were available for chlorsulfuron. To further refine the occupational and residential risk assessment, information on market data, typical use patterns and chemical-specific monitoring studies would be useful. Furthermore, modeling data used to assess the concentrations of chlorsulfuron in drinking water were considered to be conservative. Additional water monitoring data would enhance the drinking water estimations.

Recommendation for Tolerances and Registration

The residue chemistry and toxicological databases support a conditional registration and permanent tolerances for residues of chlorsulfuron *per se* in/on the following raw agricultural commodities (RACs):

Grass, forage ..... 11 ppm
Grass, hay ..... 19 ppm

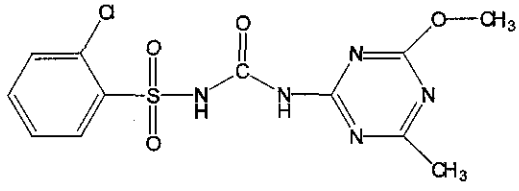
HED recommends that conversion of conditional registration to unconditional registration may be considered upon submission of the data summarized in Section 8 of this document.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

2.1 Identification of Inert Ingredient

- Chemical Name: 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino] carbonyl]benzenesulfonamide
- Common Name: Chlorsulfuron
- Chemical Type: Herbicide
- PC Code Number: 118601
- CAS Registry No.: 64902-72-3
- Empirical Formula: $C_{12}H_{12}ClN_5O_4S$
- Molecular Weight: 357.7709

2.2 Structural Formula



2.3 Physical and Chemical Properties

- Vapor Pressure: 4.6×10^{-6} mmHg at 25C
- Water Solubility: 125 ppm at 25 C
- Partition Coefficient (Octanol/Water): log K_{ow} = 1.11
- Melting Point Range: 174-178
- Relative Density: 0.63±0.05 g/ml

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Animal toxicology data are used by HED to assess the hazards to humans. The data are derived from a variety of acute, subchronic, and chronic toxicity tests; developmental/reproductive tests; and tests to assess mutagenicity and pesticide metabolism. While not complete, the existing toxicological database for chlorsulfuron supports the establishment of permanent tolerances for residues of chlorsulfuron *per se*

in/on grass forage and hay resulting from the proposed use on pasture and rangeland grasses.

The database for acute toxicity is considered incomplete. There are no acceptable data with which to assess the skin irritant and eye irritant potential of chlorsulfuron or its skin sensitizer potential. These studies are required. The available acute toxicity data indicate that chlorsulfuron is not acutely toxic *via* the oral [Toxicity Category IV], dermal [Toxicity Category III], and inhalation [Toxicity Category IV] routes of exposure (Table 1)

The database for subchronic toxicity is also considered incomplete. The 21-day repeated dose dermal toxicity study and the subchronic inhalation study are data gaps for chlorsulfuron. The subchronic oral database does not identify any particular target organ. The only treatment-related effect observed in the dog following oral exposure for 6 months was decreased body-weight gain in females, which was associated with a lower food intake. No effects were observed in the male dogs. In the subchronic toxicity study in rat, no effects were observed at the highest dose tested [161.1 mg/kg/day], which is well below the limit dose [1000 mg/kg/day]. In the subchronic mouse study, adverse effects [increased incidence of retinal dysplasia and adrenal capsular cell proliferation] were observed only at a dose level that exceeds the limit dose [2130 mg/kg/day]. Although there is no acceptable oral subchronic toxicity study in rats and mice, a chronic oral toxicity study is available in both species, and a separate subchronic oral toxicity study is not required for either species.

Adequate chronic toxicity data are available. No additional studies are required at this time. Decreased body-weight gains were observed in both sexes in the dog study. The females dogs displayed decreased erythrocyte counts and hemoglobin levels throughout most of the study, but not at study termination. No target organ was identified in either the rat or mouse study. Decreased body weight was observed in the male rats at the mid- and high-dose levels, and the high-dose males displayed a decrease in food efficiency. In the mouse, decreased body weight and body-weight gains were observed at the high-dose level in both sexes throughout the study. There was no treatment-related increase in the incidence of any tumor type in either the rat or mouse carcinogenicity study. The dose levels were considered adequate in the rat and mouse studies, based on reductions in body weight and body weight gain in the mouse and decreased body weight and food efficiency in the rat.

A complete developmental toxicity database exists for chlorsulfuron. In the rat, developmental toxicity was observed at the highest dose tested, 1500 mg/kg/day, based on decreased fetal body weight. Maternal toxicity was observed as an increased incidence of clinical signs [vaginal discharge with associated alopecia]. In the rabbit, maternal toxicity was observed as decreased body-weight gain. Developmental toxicity was indicated by decreased fetal body weight. Mortality was observed in both species at their respective high-dose levels, which were at or above the limit dose, and treatment-related abortions were observed in the rabbit study at the highest dose level also.

The database for reproductive toxicity is considered incomplete. The available 3-

generation reproductive toxicity study is classified unacceptable, and it is considered a datagap. Reproductive toxicity was observed in the F3 generation [both litters], as evidenced by decreased female fertility. Offspring toxicity was not observed. This study had numerous deficiencies including but not limited to: 1) no assessment of estrous cyclicity, sperm parameters, 2) no assessment of male reproductive performance, 3) parental animals not subjected to gross pathology or histopathology examinations, 4) no assessment of developmental landmarks, and 5) pup histopathology evaluations conducted only for the F3B generation. Although this reproduction study on chlorsulfuron conformed to the old guideline requirements, it is unacceptable under the current guideline requirement in light of the fact that most of the parameters used for FQPA assessment are not provided in the available study.

Susceptibility could not be determined in the 3-generation reproduction study because it did not meet the current guideline requirements in light of the fact that most of the parameters used for assessing susceptibility were not available (the study was conducted in 1978). Although susceptibility could not be assessed, there is confidence in the results of the study. It was determined that there is low level of concern and no residual uncertainties for the effects (decreased fertility in F3 generation) seen because there was no decrease in fertility in either the F1 or F2 generations, and the decrease in fertility seen in the F3 generation was minimal and of questionable toxicological significance at the highest dose tested (125 mg/kg/day). The HIARC determined that a 2-generation reproduction study that meets the current standards is required to meet the FQPA requirements.

No neurotoxicity studies [acute or subchronic] are available on chlorsulfuron. The HIARC Committee concluded that acute and subchronic neurotoxicity studies as well as a developmental neurotoxicity study are not required for chlorsulfuron because no evidence of neurotoxicity was found in any study on chlorsulfuron. .

Mutagenicity studies were completed over 20 years ago, and were considered incomplete based on pre-1991 and post-1991 mutagenicity guidelines. If the missing data were provided, most of the studies could be upgraded to Acceptable. In the available studies, chlorsulfuron was negative for mutagenicity in a bacterial gene mutation [Ames] assay, negative in the mammalian cell [HGPRT] gene mutation assay, negative in the CHO chromosomal aberrations assay, negative in the dominant lethal assay, and negative in the unscheduled DNA synthesis [UDS] in rat hepatocytes assay. Overall, the data suggest chlorsulfuron does not cause mutagenic effects.

Metabolism data show that chlorsulfuron is rapidly absorbed, metabolized, and excreted following oral exposure [single low, single high, and repeated low dosing regimens]. There were no remarkable sex-, dose-, or treatment-related differences in the absorption, distribution, and excretion of chlorsulfuron in rats. The major routes of elimination are the urine [58%-72%] and feces [20%-35%]. Small amounts [0.1%-0.2% of administered dose] were found in the tissues 3 days after dosing. The highest concentrations were in the liver and whole blood in both sexes. A major and a minor metabolic pathway were identified.

The major metabolic pathway was believed to be consisted of the contraction of the sulfonylurea linkage followed by oxidation and hydroxylation. The minor metabolic pathway involves the cleavage of the sulfonylurea linkage.

The carcinogenic potential of chlorsulfuron was classified as no evidence of carcinogenicity, according to EPA Guidelines for Carcinogen Risk Assessment [CFR September 24, 1986].

The toxicology profile of chlorsulfuron is shown in Table 2 of this document.

Table 1. Acute Toxicity of Chlorsulfuron Technical.

	Guideline No./Study Type	MRIDs	Results	Tox Category
870.1100	Acute oral - rat	00031406	rat LD_{50} = **5.5** g/kg ♂ rat LD_{50} = **6.3** g/kg ♀	IV
870.1200	Acute dermal - rat	00083956	rabbit LD_{50} = **3400** mg/kg	III
870.1300	Acute inhalation - rat	00086825	rat LC_{50} = **5.9** mg/L	IV
870.2400	Primary eye irritation -	00031414 ♪	not an eye irritant	IV
870.2500	Primary skin irritation -	00031414 ♪	no adequate study	-
870.2600	Dermal Sensitization	00031414 ♪	no adequate study	-

♪ classified unacceptable/nonguideline
- study not available

Table 2. Toxicity Profile of Chlorsulfuron

Guideline No.	Study Type	MRID #	Results	Core Grade
Subchronic Toxicity				
870.3100 [§82-1 (a)]	Subchronic **oral** - Rats (90 days) 100, 500, 2500 ppm males 6.5, 33.7, 161.1/ females 8.1, 40.4, 216.6 mg/kg/day	MRID: 00031418 [1980]	**Chlorsulfuron (≈95% a.i.)** NOAEL: 161.1 mg/kg/day [2500 ppm; HDT]. No effects were observed. Dosing inadequate; well below the limit dose	Unacceptable/Guideline, it does not satisfy guideline.
870.3150 [§82-1 (b)]	Subchronic **oral** - Dogs (6 months) 100, 500, 2500 ppm [3.7, 18.5, 82.3 mg/kg/day]	MRID: 00031420 [1980]	**Chlorsulfuron (95% a.i.)** NOAEL: 18.5 mg/kg/day, based on decreased body weight/body-weight gain at the LOAEL of 82.3 mg/kg/day.	Acceptable/non-guideline
870.3100 [§82-1 (a)]	Subchronic **oral** - Mice (90 days) 500, 2500, 5000, 7500 ppm [males 150, 783, 1557, 2130/females 220, 1214, 2134, 3176 mg/kg/day]	00031421 [1980]	**Chlorsulfuron (100% a.i.)** NOAEL: 1557 mg/kg/day, based on an increased incidence of retinal dysplasia and adrenal capsular cell proliferation at the LOAEL of 2130 mg/kg/day.	Unacceptable/Guideline, it does not satisfy guideline.
Chronic Toxicity/Carcinogenicity				
870.4100 [§83-1b]	Chronic feeding study in beagle dogs 100, 2000, and 7500 ppm [males 3.5, 65.6, and 215/females 3.5, 60.6, and 254.5 mg/kg/day for m2 weeks]	41862602 [1991	**chlorsulfuron (97.5% a.i.)** NOAEL: 60.6 mg/kg/day LOAEL: 215 mg/kg/day, based on decreased body-weight gain, erythrocyte counts, and hemoglobin levels	Acceptable/Guideline
870.4200 [§83-2]	Carcinogenicity study -CD-1 mice [0, 100, 500, 5000 ppm [0, 15, 108, 750 mg/kg/day] for 104 weeks	00090030 [1981]	**chlorsulfuron (95% and 91.9%)** NOAEL = 500 ppm [108 mg/kg/day] LOAEL: 5000 [750 mg/kg/day], based on decreased body weight and body-weight gain. There was no treatment-related increase in tumor incidence in either sex.	Acceptable/Guideline
870.4300 [§83-5]	Chronic feeding/carcinogenicity study CD® rats [0, 100, 500, and 2500 ppm (0, 5, 25, and 125 mg/kg/day] for 2 years.	MRID 00086003 [1981]	**chlorsulfuron (>95% a.i.)** NOAEL: 50 ppm [5 mg/kg/day] LOAEL: 500 ppm [25 mg/kg/day], based on decreased body weight in males There was no treatment-related increase in tumor incidence in either sex.	Acceptable/Non-guideline

Guideline No.	Study Type	MRID #	Results	Core Grade
Developmental Toxicity				
870.3700 [§83-3a]	Developmental Toxicity - Crl:CD®(SD)BR rats [0, 55, 165, 500, and 1500 mg/kg/day]	41976406 [1991]	**chlorsulfuron (98.22% a.i.)** Maternal NOAEL: 165 mg/kg/day Maternal LOAEL: 500 mg/kg/day, based on clinical signs [vaginal discharge with associated alopecia. At HDT, there were two deaths [GD 12 and 18], and additional clinical signs [swollen limbs and faces]. Developmental NOAEL: 500 mg/kg/day Developmental LOAEL: 1500 mg/kg/day, based on decreased fetal body weight.	Acceptable/Guideline
870.3700 [§83-3b]	Developmental Study - Hra:(NZW)SPF Rabbits [0,25, 75, 200, 400 mg/kg/day (original study); 400 and 1000 mg/kg/day (supplemental study)]	41983101 [1991]	**chlorsulfuron (98.2% a.i.)** Maternal NOAEL: 75 mg/kg/day Maternal LOAEL: 200 mg/kg/day, based on decreased body-weight gain. At HDT, there were 8/20 deaths and 6 abortions. Developmental NOAEL: 200 mg/kg/day Developmental LOAEL: 400 mg/kg/day, based on a slight increase in visceral malformations and decreased fetal body weight.	Acceptable/Guideline
Reproductive Toxicity				
870.3800 [§83-4]	3-Generation Reproduction Toxicity in CD® Rats 0, 100, 500, 2500 ppm [0, 5, 25, 125 mg/kg/day	00086003 [1981]	**chlorsulfuron (95%-95.9% a.i.)** Parental NOAEL: 2500 ppm [125 mg/kg/day] Parental LOAEL: >2500 ppm [125 mg/kg/day], no effects observed. Reproductive NOAEL: 100 ppm [5 mg/kg/day] Reproductive LOAEL: 500 ppm [25 mg/kg/day], based on decreased female fertility. Offspring NOAEL: 2500 ppm [125 mg/kg/day] Offspring LOAEL: >2500 ppm [125 mg/kg/day], no effects observed.	Unacceptable/non-guideline
Neurotoxicity				
870.6200 [§81-8]	**acute neurotoxicity study is not required**			

Guideline No.	Study Type	MRID #	Results	Core Grade
870.6200 [§82-7]	**subchronic neurotoxicity study is not required**			
Metabolism				
870.7485 [§85-1]	Metabolism	42540701 [1989]	Chlorsulfuron is rapidly absorbed, metabolized, and excreted following oral exposure [single low, single high, and repeated low dosing regimens]. There were no remarkable sex-, dose-, or treatment-related differences in the absorption, distribution, and excretion of chlorsulfuron in rats. The major routes of elimination are the urine [58%-72%] and feces [20%-35%]. Small amounts [0.1%-0.2% of administered dose] were found in the tissues 3 days after dosing. The highest concentrations were in the liver and whole blood in both sexes. A major and a minor metabolic pathway were identified.	Acceptable/guideline
Mutagenicity				
870.5100.	Ames, reverse mutation;	00031425	6-30 μg/plate w/ w/out S9 in *S. Typhimurium* strains TA1535, TA1537, TA1538, TA98, TA100. **No evidence of induced mutant colonies over background.** Can be upgraded.	Unacceptable
870.5300.	Mammalian cells in culture - gene mutation [HGPRT]	00083943	0.028-2.8 mM, w/ and w/out S9 mix. No cytotoxicity at solubility limit w/ and w/out S9. **No evidence of induced mutant colonies over background.** Can be upgraded.	Unacceptable
870.5385.	*in vitro* cytogenetics assay; chromosome aberration [CHO-WBI cells];	00088755	16.7-5000 μg/mL [8.5-10 hours w/out S9; 2 hours w/ S9]. Marked cytotoxicity at 5000 μg/mL. **No evidence of chromosomal aberrations.**	Acceptable
870.5450.	dominant lethal assay	00083944	100, 500, 5000 ppm in diet of male CD® Sprague-Dawley rats for 10 weeks. **No difference between control and treated rats in any reported parameter.** Purity of test material not provided. No justification for dose levels. No concurrent or positive control data.	Unacceptable
870.5450.	Unscheduled DNA synthesis primary rat hepatocyte assay;	00090008	initial 0.0002-2.0 mg/mL, confirmatory 0.0004-4.0 mg/mL; adult male F344 primary rat hepatocytes [18 hours]; at ≥0.4 mg/mL too cytotoxic to evaluate **No evidence that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced. .** Purity of test material and # of cells scored for UDS not provided. Can be upgraded with this information.	Unacceptable

NOAEL = No Observable Adverse Effect Level
LOAEL = Lowest Observable Adverse Effect Level
LDT = Lowest Dose Tested; HDT = Highest Dose Tested
ChE = Cholinesterase

3.2 Dose Response Assessment and Hazard Endpoint Selection

The strengths and weaknesses of the chlorsulfuron toxicology database were considered during the process of toxicity endpoint and dose selection. The toxicology database for chlorsulfuron is not complete. There are data gaps for the 21-day dermal and subchronic inhalation toxicity and the 2-generation reproduction studies in rats. Although several key studies are required to be submitted, information gathered from the available studies provided reasonable confidence when the toxicity endpoints and doses for risk assessment were selected. Based on the evaluation of the above summarized studies, the HIARC identified the toxicity endpoints and the dose levels for use in risk assessment (HIARC document of 7/17/02, TXR# 0050920). The selected toxicity endpoints are summarized in Table 3. There are no dermal-absorption studies available for review. Consequently, toxicity by the dermal route was considered to be equivalent to toxicity via the oral route of exposure.

Table 3. Summary of Toxicological Dose and Endpoints for CHLORSULFURON for Use in Human Risk Assessment

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13-50 years of age	no appropriate endpoint for this exposure scenario was identified		
Acute Dietary general population including infants and children	no appropriate endpoint for this exposure scenario was identified		
Chronic Dietary all populations	NOAEL= 5 mg/kg/day UF = 300 Chronic RfD = 0.02 mg/kg/day	FQPA SF = 1 cPAD = chronic RfD / FQPA SF = 0.02 mg/kg/day	rat chronic toxicity/carcinogenicity LOAEL = 25 mg/kg/day based on decreased body weight in males
Incidental Oral, Short-Term Residential Only	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain
Incidental Oral, Intermediate-Term Residential Only	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain.
Short-Term (Dermal) [a]	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Endpoint for Risk Assessment	Study and Toxicological Effects
Intermediate-Term (Dermal) [a]	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain
Long-Term (Dermal) [a]	NOAEL = 5 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	chronic toxicity/carcinogenicity study in rats LOAEL = 25 mg/kg/day based on decreased body weight in males
Short Term (Inhalation) [b]	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain
Intermediate Term (Inhalation) [b]	NOAEL = 75 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	developmental toxicity study in rabbits LOAEL = 200 mg/kg/ day based on decreased body-weight gain
Long Term (Inhalation) [b]	NOAEL = 5 mg/kg/day UF = 300	FQPA SF = 1 LOC for MOE = 300 (residential only) LOC of MOE = 100 (occupational)	chronic toxicity/carcinogenicity study in rats LOAEL = 25 mg/kg/day based on decreased body weight in males

[a] An oral NOAEL/LOAEL was selected. In the absence of adequate dermal absorption data, absorption *via* the dermal route is assumed to be equivalent to oral absorption. [b] An oral NOAEL/LOAEL was selected. In the absence of adequate inhalation absorption data, absorption *via* the inhalation route is assumed to be equivalent to oral absorption.

[b] UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern.

3.3 FQPA Considerations

The Health Effects Division (HED) FQPA Safety Factor Committee (SFC) met on June17, 2002 and again on July 12, 2002 (electronically) to evaluate the hazard and exposure data for chlorsulfuron with regard to making a decision on the additional safety factor for the protection of infants and children. The HIARC, in accordance with the 2002 OPP 10X Guidance Document, had concluded that an additional 3X database uncertainty factor (UF) is needed for data deficiencies in the toxicology database of chlorsulfuron (an acceptable 2-generation reproduction study). An UF of 3X (as opposed to a 10X) is adequate because the chronic RfD is based on the NOEL of 5 mg/kg/day, which is 5X lower than the conservative NOAEL of 25 mg/kg/day established and could be 25X lower if the NOAEL is established at 125 mg/kg/day in the existing 3-generation reproduction study (as discussed above). The SFC concurred with the HIARC that reliable data demonstrate that the safety of infants and children will be protected by use of an additional database uncertainty factor of 3X.

The SFC also concluded that no Special FQPA safety factor was needed for several reasons.

- The toxicology database for chlorsulfuron contains acceptable guideline developmental studies which show no quantitative or qualitative evidence of increased susceptibility following *in utero* exposure. The HIARC concluded that there are no residual uncertainties for prenatal toxicity in the acceptable guideline developmental studies with chlorsulfuron. Although susceptibility could not be assessed in the unacceptable reproduction study, this uncertainty has been accounted for by the application of a database uncertainty factor. The chronic RfD and the toxicity endpoints established are protective of pre/postnatal toxicity.

- There are no residual uncertainties identified in the exposure databases. The dietary food exposure assessment includes tolerance level residues and assumes that 100% of crops were treated with chlorsulfuron. Dietary drinking water exposure is based on a worst-case scenario (direct application to water) which includes all degradates. The residential post-application assessment is also considered to be very conservative since it uses the Residential SOPs and assumes that the entire time spent on the lawn was on the 'spot-treated' area. These exposure assessments will not underestimate the potential exposure to infants and children resulting from the use of chlorsulfuron.

3.4 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 the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases 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 FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has 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 the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, chlorsulfuron may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT AND CHARACTERIZATION

4.1 Summary of Proposed Uses

Chlorsulfuron is a selective herbicide currently registered for use on barley, oats, and wheat at a maximum label use rate of 0.375 oz a.i./A. The petitioner provided supplemental labeling for the 75% DF formulation (EPA No. 352-522; Product Name = TELAR™ DF Herbicide) proposed for weed control in pasture, range and conservation reserve program (CRP) lands. For the proposed use on grasses, chlorsulfuron is intended to be applied to grass, once, as a broadcast spray at 1.0 oz ai/acre when grass is at its forageable stage just prior to booting. A zero day PHI is proposed. Treatments may be applied by ground equipment or aerially. The label recommends that the highest application rate (1.0 oz a.i./A) be applied only as a spot treatment because of phytotoxicity issues. Prebloom to bloom and fall rosette are the recommended timings. TELAR™ DF may not be applied through any type of irrigation system. A summary of the directions for use is shown in Table 4.

Table 4. Summary of Directions for Use of Chlorsulfuron on Grass (Pasture and Rangeland).

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (oz ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (oz ai/A)	PHI (days)	Use Directions and Limitations
Prebloom to bloom or fall rosette ground or aerial broadcast spray	75% DF* (352-522)	1.0 oz	1	1.0 oz	0	Use maximum rate only for spot treatment. Do not apply by chemigation

*DF = Dry Flowable

4.2 Dietary Exposure/Risk Pathway

4.2.1 Residue Profile

The residue chemistry database for chlorsulfuron is substantially complete. Adequate data were submitted in support of the tolerances for residues of chlorsulfuron on grass. No deficiencies have been noted which would impinge on the establishment or reassessment of tolerances for chlorsulfuron. The geographic representation and number of trials for pasture grass are adequate. Chlorsulfuron residues ranged from 1.2 to 11 ppm in/on forage and ND (<0.05 ppm) to 19 ppm in/on hay treated with chlorsulfuron at the maximum proposed use rate of 1.0 oz ai/A and a minimum preharvest interval of 0 days. Treated samples were stored frozen (-20 $\pm$ 5 °C) for up to 15.6 months.

Nature of the Residue

The nature of the residue in small grains is adequately understood. Data submitted in support of reregistration indicated extensive metabolism in wheat within 19 days of treatment. Residues identified in wheat include parent, the 5-hydroxy metabolite and its glucose conjugate, and a number of minor metabolites. Total radioactive residues in mature straw and grain samples treated at the 1X rate were <0.01 ppm, below levels that would require characterization. The HED Metabolism Committee (D213898, 4/11/95) concluded that the residue to be regulated in plants was chlorsulfuron parent only.

The petitioner requested a waiver of data which determines the nature of the residue of chlorsulfuron in pasture and rangeland grasses. Chlorsulfuron application to grasses as well as to wheat and barley are as broadcast applications, pre- and postemergent using ground or aerial equipment. The Chemistry Science Advisory Council on January 31, 2002 determined that the waiver be granted since the application method proposed for grasses is the same as the method used in the wheat and barley studies and metabolism is expected to be very similar amongst members of the grass family which includes small grains. Additional nature of the residue studies may be required if new uses are proposed.

The nature of the residue in ruminants is also adequately understood. Goats were fed 25 ppm chlorsulfuron, representing approximately 0.5x the expected dietary burden, based on present tolerances in small grains. Parent was the major residue in milk and kidney, the tissues with the highest total radioactive residues (TRR). 2-Chloro-benzenesulfonamide and the methoxy methyl triazine amine were also identified in goat tissues. Parallel studies were conducted with ^{14}C labeled either uniformly in the phenyl ring or at the 2 position (the carbon connected to the urea group) in the triazine ring. Metabolites formed after cleavage of the sulfonyl urea bridge were identified in samples with one label or the other, but not both.

The nature of the residue in poultry is adequately understood. Laying hens were fed 46 ppm chlorsulfuron, representing about 460X the expected dietary burden, based on present tolerances in small grains. As with the studies in ruminants, parallel studies were conducted with ^{14}C label either uniformly in the phenyl ring or at the 2 position in the triazine ring. Residues identified include parent chlorsulfuron, along with O-desmethyl-chlorsulfuron, 2-chloro-benzenesulfonamide, 2-chloro-5-hydroxy-benzenesulfonamide, 4-methoxy-6-methyl-triazine urea, and 4-methoxy-6-methyl-triazine amine. Residues in tissues based on the poultry dietary burden are not expected to be detectable.

The Metabolism Committee (D217473, 8/9/95) determined that there was no toxicological concern over metabolites at the levels identified in poultry and that tolerances for livestock should continue to be expressed as residues of parent chlorsulfuron only.

Analytical Methods

Residues of chlorsulfuron in pasture grasses were determined based on procedures described in Du Pont study no. AMR 3822-96, "Analytical Method for the Determination of Chlorsulfuron in Wheat (Forage, Grain, and Straw) and Grass (Forage and Hay) by EI-LC/MS". This method was determined to be adequate for data collection (K. Dockter, D 251814, 1/10/2000). Briefly, this method consists of aqueous extraction of chlorsulfuron from wheat and grass matrices, and purification by solid phase extraction [SPE] using a C18 packing material. Clean-up was followed by HPLC on a 4.6 mm x 25 cm cyanopropyl column. MS detection was carried out in a positive ion mode using electrospray ionization. The chlorsulfuron parent/daughter ion pair, 358.2-> 141.0 were monitored. The limit of detection (LOD) and limit of quantitation were determined to be 0.02 ppm and 0.05 ppm, respectively.

Methods are available for the enforcement of tolerances for chlorsulfuron residues in/on plant and animal commodities. PAM Vol. II lists Methods I and II, HPLC methods with photoconductivity detection (PCD), for the determination of chlorsulfuron residues in plants and livestock commodities and milk.

A new enforcement method provided by the petitioner intended to replace the existing Pesticide Analytical Manual (PAM) Methods I and II methods, was submitted for Agency validation. The Agency found the petitioner's proposed method for plants to be inadequate as an enforcement method. Accordingly, HED recommended that the Registrant either develop a simpler method, as recommended by the Analytical Chemistry Section, BEAD, or radiovalidate the existing enforcement method in PAM, Vol. II for residues of parent chlorsulfuron only using samples from the wheat metabolism study. These recommendations remain in effect. Preferred samples for radiovalidation are Day 0 samples treated at the 1X rate. The proposed enforcement analytical method for livestock tissues and milk was found to be adequate for enforcement by the Agency.

PAM, Vol. I, Appendix II (1/94) describes FDA Multiresidue Protocols A through G, and a decision tree for MRM testing. Vol. I, Appendix I reports that chlorsulfuron is not recovered by methods described in Sections 303 and 304, corresponding to Protocols E and F, respectively. Data are required on the remaining Protocols, depending on their applicability to chlorsulfuron.

Storage Stability

Treated samples were stored at -20 C for no longer than 15.6 months between sampling and extraction. Results of the storage stability study showed that chlorsulfuron is stable in wheat hay and forage for up to 16.3 months and in pasture

grass hay and forage for up to 16.2 months. The requirements for storage stability are fulfilled; no additional data are required.

Meat, Milk, Poultry, and Eggs

A ruminant feeding study was reviewed in the Chlorsulfuron Registration Standard dated October 8,1982. Three groups of two cows were fed 2, 10, and 50 ppm of chlorsulfuron for 28 days. A fourth group of two cows were kept as controls. Twenty-four hours after the last treatment, one cow from each group was sacrificed and samples of blood and various tissues were taken. The remaining cow in each feeding group was withdrawn from chlorsulfuron for 8 days and then sacrificed. Milk was sampled daily with one sample each week being separated into cream and skim milk fractions. Residues of chlorsulfuron per se in composited (AM and PM) whole milk samples were <0.01 ppm at the 2 ppm feeding level, <0.01 to 0.019 ppm at the 10 ppm feeding level, and 0.021 to 0.10 ppm at the 50 ppm level. Residues in milk decreased to <0.01, <0.01 and 0.072 ppm for the 2, 10, and 50 ppm feeding levels respectively, within 24 hours of withdrawal from chlorsulfuron. All milk samples showed <0.01 ppm of chlorsulfuron after 48 hours of withdrawal. Residues in milk plateaued at ~3 days after initiation of the feeding study. Residues of parent, chlorsulfuron, in various tissues ranged from <0.01 ppm to 0.26 ppm in the cow fed 10 ppm of chlorsulfuron and ranged from <0.01 to 0.25 ppm in the cow fed 50 ppm of chlorsulfuron. The highest residues were observed in liver and kidney.

The ruminant feeding study is supported by storage stability studies and the analytical method is adequate for enforcement of meat and milk tolerances.

HED Metabolism Committee concluded that a poultry feeding study and poultry and egg tolerances are not required based on no toxicological concerns for residues in poultry at the levels detected. The waiver was contingent on there being no increase in the tolerance levels in small grains. (D213955, 5/8/95, J. Abbotts). The proposed use on pasture and rangeland grass does not impact this decision since grass is not a poultry feed item.

The maximum theoretical dietary intake of chlorsulfuron by cattle and swine is approximately 46 ppm and 0.1 ppm, respectively. Based on the results of the feeding study, residues are not likely to exceed the current meat and milk tolerances of 0.3 ppm (meat, fat, meat byproducts) and 0.1 ppm (milk).

Crop Field Trials

Residue data reflecting the proposed use on pasture and rangeland grasses were submitted by the petitioner and found to be adequate. In studies conducted in Regions 1, 2, 3, 4, 6, 9, 10, 11, & 12, chlorsulfuron residues found in pasture grass forage and hay ranged from 0.75-3.9 ppm and 0.80-11 ppm, respectively at Day 0

following application - during forageable growth stage - at 0.50 oz ai/A. After application at 1.0 oz ai/A (1X), residues found in forage ranged from 1.2-11 ppm, <0.05-1.4 ppm, and <0.05-0.77 ppm at Day 0, 7, and 14, respectively. Corresponding values for hay were 1.0-19 ppm, 0.098-3.6 ppm, and <0.05-1.4 ppm. Residues found in forage and hay ranged from 0.09-3.0 ppm and 0.26-10 ppm, respectively, at Day 7 following application at 2.25 oz ai/A. In another submission, chlorsulfuron was applied to pasture grass once at a rate of 1.0 oz a.i./acre (1X). The field trials were conducted in Regions 5, 7 and 8. Samples were collected at 0 and 7 day PHIs. Chlorsulfuron residues ranged from 1.9 to 4.8 ppm in/on forage and 4.5 to 15 ppm in/on hay treated with chlorsulfuron at the 0 day PHI.

For all trials, samples were analyzed for residues of chlorsulfuron using a LC/MS method described in Du Pont study no. AMR 3822-96, "Analytical Method for the Determination of Chlorsulfuron in Wheat (Forage, Grain, and Straw) and Grass (Forage and Hay) by EI-LC/MS" which was discussed previously in this document.

The data requirements for the proposed use of chlorsulfuron on pasture and rangeland grasses are fulfilled. The geographic representation and number of trials for grasses (pasture and rangeland) are adequate. Additional field trial data are not required.

Processed Food and Feed

There are no processed food items associated with this proposed use.

Confined Accumulation in Rotational Crops

The requirements of Guideline 860.1850, Confined Rotational Crops, have been met. The available confined rotational crop data indicate that ^{14}C-residues were <0.05 ppm in/on all rotational crop commodities of wheat, sugar beets, and rape planted 4 and 12 months following applications of [^{14}C]chlorsulfuron to silt loam soil at a rate of 1 oz ai/A (1X). Detectable residues of parent (≤0.2 ppb) were not found.

Provided plantback intervals of 4 months or longer are specified on all labels allowing crop rotation, no tolerances are required for rotational crops. The confined accumulation in rotational crop studies indicate that limited field studies are not required.

Water, Fish, Irrigated Crops and Food Handling Establishments

Chlorsulfuron is not registered for direct use on water and aquatic food and feed crops or in food-handling establishments; therefore, no residue chemistry data are required under these guideline topics.

Proposed Tolerances

Tolerances are currently established for the combined residues of chlorsulfuron, 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]benzenesulfonamide and its metabolite 2-chloro-5-hydroxy-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]benzenesulfonamide, in or on barley, oats and wheat ranging from 0.1(grain) to 20 ppm (forage) [40 CFR 180.405(a)]. Tolerances are also established for residues of the parent, chlorsulfuron, in or on meat, fat, and meat byproducts at 0.3 ppm and milk at 0.1 ppm (see Table 5). The HED Metabolism Committee has determined that the residue to be regulated in plants and livestock is the parent only [D213898, 4/11/95, J. Abbotts (plants) and D217473, 8/9/95, J. Abbotts (livestock)]. Tolerances of 11 and 19 ppm have been proposed for grass forage and hay, respectively and are adequately supported by residue data.

The tolerance expression should be changed to reflect the recommendations of the HED Metabolism Committee. No changes to the tolerance level are required as a result of deleting the metabolite from the tolerance expression.

There are no Codex, Canadian, or Mexican MRLs; therefore, issues of compatibility do not exist.

Table 5. Tolerance Summary for Chlorsulfuron

Commodity	Established/Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Grass, Forage	N/A	11	None
Grass, Hay	N/A	19	None
Barley, grain	0.1	0.1	None
Barley, straw	0.5	0.5	None
Oat, Forage	20.0	20.0	None
Oat, Grain	0.1	0.1	None
Oat, Straw	0.5	0.5	None
Wheat, forage	20.0	20.0	None
Wheat grain	0.1	0.1	None
Wheat, straw	0.5	0.5	None
Cattle, fat	0.30	0.30	None
Cattle, meat	0.30	0.30	None

Commodity	Established/Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Cattle meat byproducts	0.30	0.30	None
Goats, fat	0.30	0.30	None
Goats, meat	0.30	0.30	None
Goats, meat byproducts	0.30	0.30	None
Hogs, fat	0.30	0.30	None
Hogs, meat	0.30	0.30	None
Hogs, meat byproducts	0.30	0.30	None
Horses, fat	0.30	0.30	None
Horses, meat	0.30	0.30	None
Horses, meat byproducts	0.30	0.30	None
Milk	0.10	0.10	None
Sheep, fat	0.30	0.30	None
Sheep, meat	0.30	0.30	None
Sheep, meat byproducts	0.30	0.30	None

4.2.2 Dietary Exposure Analyses

HED conducts dietary (food only) risk assessments using DEEM™, ver 7.76, which incorporates consumption data generated in USDA's CSFII, 1989-1992. For chronic risk assessments, residue estimates for foods or food-forms of interest are multiplied by the average consumption estimate of each food/food-form of each population subgroup. Chronic exposure estimates are expressed in mg/kg bw/day and as a percent of the cPAD.

4.2.2.1 Acute Dietary Exposure Analysis

Acute doses and endpoints were not selected for the general U.S. population (including infants and children) or the females 13-50 years old population subgroup for chlorsulfuron; therefore, an acute dietary exposure analysis was **not** performed.

4.2.2.2 Chronic Dietary Exposure Analysis

A conservative chronic analysis was performed using the HED-recommended tolerance level residues, and 100 % crop treated with chlorsulfuron. For chronic dietary risk, HED's level of concern is >100% cPAD. Dietary exposure estimates for representative population subgroups are presented in Table 6. Results of the dietary analyses showed exposure to chlorsulfuron consumed no more than 8% of the chronic PAD. The highest exposed population subgroup was children 1 to 6 years old.

Table 6. Summary of Results from Chronic DEEM™ Analysis of Chlorsulfuron.

Subgroup	Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	0.001310	3
All Infants (< 1 year old)	0.001458	3
Children 1-6 years old	0.003869	8
Children 7-12 years old	0.002232	5
Females 13-50 years old	0.000857	2
Males 13-19 years old	0.001442	3
Males 20+ years old	0.000914	2
Seniors 55+ years old	0.000778	2

HED notes that there is a degree of uncertainty in extrapolating exposures for certain population subgroups that may not be sufficiently represented in the consumption surveys, (e.g., nursing and non-nursing infants). However, risk estimates for these subpopulations are included in representative populations having sufficient numbers of survey respondents (e.g., all infants). The population subgroups listed in Table 4 are subgroups having a sufficient number of respondents in the USDA 1989-92 CSFII food consumption survey to be considered statistically reliable.

4.2.2.3 Cancer Dietary Exposure Analysis

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July, 1999), the HIARC classified chlorsulfuron as "no evidence of carcinogenicity" based upon lack of evidence of carcinogenicity in rats and mice. Therefore, a cancer dietary exposure analysis was not performed.

4.3 Water Exposure/Risk Pathway

The following information concerning the environmental fate and drinking water

assessment of chlorsulfuron was provided by EFED (Drinking Water Assessment to Support TRED for Chlorsulfuron, L Shanaman, 25-JUN-2002). At the present time, surface and ground water monitoring data are not available. *The Pesticides in Groundwater Database, A Compilation Of Monitoring Studies: 1971-1991 National Summary*, US EPA September 1992, entries indicate that of eight wells tested, there were no recorded detections of chlorsulfuron. While chlorsulfuron is not predicted to be persistent in the environment, it is expected to be very mobile. Agricultural uses would impact surface water supplies most heavily in Kansas, Oklahoma, Northern Texas, the Pacific Northwest, and populated areas downstream of those locations. Applications of chlorsulfuron to rights-of-way and industrial sites pose an undetermined degree of exposure to population in areas surrounding the use sites.

A conservative estimate of surface water EEC's and drinking water concentrations were made which would included any possible degradation products. While laboratory data did indicate that some of the degradation products were less mobile than the parent, the results were unquantified. A conservative estimate of degradate mobility equal to that of the parent compound, chlorsulfuron, was made. In the absence of any quantified biotic or abiotic degradation data for the transformation products, which generally reached the reported maximum at study termination, complete stability was assumed for both parent and the degradates. This assumption assured that both the parent compound and the degradation products would be included in the estimated surface water concentrations. The modeling results from FIRST, using these assumed parameters, estimates pre-treatment surface water concentrations of *total chlorsulfuron residues (both parent and degradation products)*, resulting from two applications, at 60 day intervals, of the maximum use rate of LESCO TFC Dispersible Granule Turf Herbicide, at an acute (peak) value of 59.7 ug/L (ppb), and a chronic (average annual) value of 41.3 ug/L (ppb).

4.4 Residential Exposure/Risk Pathway

According to registered labels, chlorsulfuron can be used on lawns to control perennial "bunch or clump" grasses or other weeds. Since it is not a restricted chemical, residential/homeowner handlers can apply it to lawns.

Chlorsulfuron use on lawns was assessed at the maximum label rate for residential handler and postapplication exposure risk calculations. The directions indicate use as a spot treatment on turf with, "a rate of 1.0 to 5.33 ounces per acre to cover 725 to 4000 sq.ft depending upon weed species." This wording should be rewritten to be equivalent to 0.25 lb ai/ A or 0.0057 lb ai/1000 sq ft.. According to the registered formulations, chlorsulfuron is only marketed as a water dispersible granule. HED assumes only adult handlers apply pesticides in the residential environment.

Residential exposure risk was assessed using standard values and assumptions from the Residential Exposure Assessment Standard Operating Procedures (ResSOPs, September 1999). The ResSOPs were further described for use in risk assessments in HED Science Advisory Committee on Exposure (ExpoSAC) Revised Policy 012 (February 22, 2001).

Residential handlers are assumed to be wearing short sleeved shirts, and short pants. The unit exposure values listed in the ResSOPs for common types of home equipment have varying degrees of "representativeness" depending on the PHED study monitoring protocol, the grade of data and confidence. The scenarios listed below were used for this exposure risk assessment and are the best available for uses of chlorsulfuron.

(1) Low Pressure Handwand: Mixer/loader/applicator
(2) Backpack Sprayer: Mixer/loader/applicator

The following assumptions were used for the residential handler and postapplication exposure risk calculations. Most of these assumptions were taken from the ResSOPs and ExpoSAC policy 12 and were characterized as high-end assumptions (conservative).

* Maximum rate used on lawn spot treatment,
* Adult weighs 70 kg, toddler weighs 15 kg,
* Mixer/loader is adult and would also apply product,
* Contact with only treated turf on day of treatment,
* 5% of application rate available for transfer from treated turf to wet hands,
* The hand-to-mouth surface area has been defined by the SAP as 1 to 3 fingers (5.7 to 17.1 cm^2) a screening level of 20 cm^2 was selected based on the assumption that each hand-to-mouth event equals 3 fingers.
* The 1999 SAP recommended the use of the 90^{th} percentile value of hand to mouth events of 20 events per hour per Reed et al., (1999). Median reported in that study was 9.5 events.
* There is incomplete removal of residues on the hands water or saliva, for screening purposes, the value of 50% is recommended.
* 2 hours per day of playing outdoors on grass represents the 75^{th} percentile of time (EPA Exposure Factors Handbook).

4.4.1 Residential Handler Exposures and Risk

According to the risk calculations, the exposure risk for residential handlers is not of concern (MOE>300). Table 7 contains the results of residential handler exposure risk calculations.

Table 7: Residential Handler Exposure Risk for Chlorsulfuron: Turf Application

Product% AI	Rate of Product (oz/A)	lb ai / 1000 ft² [a]
75	5.33	**0.0057**
Spot treatment : Res SOPs;		

Handler	Dermal					Inhalation				Combined MOE[e]
	Unit (mg/lb ai)	Area Treated (ft²)	Exposure[b] (mg/day)	Dose[c] (mg/kg/day)	MOE[d]	Unit (μg ai/lb)	Exposure[b] (mg/day)	Dose[c] (mg/kg/day)	MOE[d]	
Low Pressure Handwand	103.6	1000	0.59	0.01	8800	21.6	1.2e-03	1.8e-06	4.2e+07	8800
Garden: Backpack Sprayer	4.9		0.028	0.00040	190000	30	1.7e-04	2.5e-06	3.7e+07	190000

a Application Rate (lb ai / 1000 ft²) = $\frac{5.33 \text{ oz product} * (75\%) * \text{lb}}{1\text{A} * 100\% * 16 \text{ oz}} * \frac{1A}{43.56 Ksqft}$

b Exposure (mg/day) = Unit (mg/lb ai or μg ai/lb) * Application Rate (lb ai / 1000 ft²)* Area Treated [(ft²)/ day] [* 1000 μg/mg conversion if necessary].

c Dose[c] (mg/kg/day) = $\frac{\text{Exposure (mg/day)* Absorption Factor (Dermal or Inhalation)}}{\text{Body Weight (70 kg)}}$

Dermal and Inhalation Absorption Factor = 1 for chlorsulfuron.

d MOE = $\frac{NOAEL(mg/kg/day)}{Dose(mg/kg/day)}$;

NOAEL = 75 mg/kg/day for short and intermediate dermal and inhalation exposures. Target MOE = 300.

e Combined MOE = $\frac{1}{\left(\frac{1}{MOEdermal} + \frac{1}{MOEinhalation}\right)}$ Target Combined MOE = 300.

4.4.2 Residential Postapplication Exposure and Risk

Residential postapplication exposure to treated lawn was assessed for adults and toddlers. Standard values were used to represent the amount of applied active ingredient available for exposure (percent dislodgeable), contact surface area, saliva extraction, events per hour, time per day and transfer coefficient (ExpoSAC policy 12). Residential pesticides were assumed to be contacted by adults and children on the day of application (DAT 0). According to the exposure risk calculations, postapplication exposure risk was not of concern (MOEs range between 770 and 80,000) (Table 8).

Toddler postapplication exposure was calculated for dermal and oral exposures. Since the incidental oral and dermal short-term endpoints were the same, the MOEs were combined in an aggregate MOE. The aggregate MOE for postapplication toddler exposure risk was 740, therefore not a risk of concern (target MOE = 300).

Table 8: Residential Postapplication Exposure Risk for Chlorsulfuron (Toddler and Adult).

Postapplication Residential Exposure Risk										
Postapp	Rate (lb ai/1000 ft^2)	Rate[a] (mg ai/ cm^2)	Dislodgeable[b] of Applied)	Surface Area[b] (cm^2)	Saliva Extraction[b]	Events/hr[b]	Hours/day	Exposure[b] (mg/day)	Dose[c]	MOE[d]
Toddler										
Dermal	0.0057	0.0028	5%	5200	1	1	2	1.5	0.097	770
Hand to Mouth	0.0057	0.0028	5%	20	0.5	20	2	0.056	0.0037	20000
Object to Mouth	0.0057	0.0028	20%	25	1	1	1	0.014	0.00093	80000
Soil Ingestion	0.0057	0.0028	100%	1	1	1	1	0.0028	0.00019	400000
Adult										
Dermal	0.0057	0.0028	0.05	14500	N/A	N/A	2	4.1	0.058	1300

a Rate (mg ai/ cm^2) = Rate (lb ai/1000 ft^2) * 454000 (mg/lb) * 1 ft^2/ 929 cm^2.

b ResSOP, ExpoSAC Policy 12.

c $$\text{Exposure (mg/day)} = \frac{\text{Rate (mg ai / cm2)} * 5\% * SalivaExtraction50\%}{100\%} * \frac{20event}{hr} * \frac{2hours}{day} * \text{Contact Surface area (cm}^2\text{)}.$$

d Dose[c] (mg/kg/day) =

Dermal and Inhalation Absorption Factor = 1 for chlorsulfuron.

e $$\text{MOE} = \frac{NOAEL(mg/kg/day)}{Dose(mg/kg/day)}$$; NOAEL = 75 mg/kg/day for short and intermediate dermal exposures.

The chlorsulfuron residential exposure risk assessment should be considered conservative. Use of chlorsulfuron in residential settings was not quantified by any source, however label language suggests minimal residential marketing. The ResSOP scenarios used to estimate potential exposure are "best fit" for uses of chlorsulfuron. Given the low use rates, minimal re-applications (60 day interval) and high end values from ResSOPs this assessment should be considered conservative.

4.4.3 Summary of Postapplication Spray Drift/Track-In Risks

HED has concerns for the potential for children's exposure in the home as a result of agricultural uses of chlorsulfuron. Environmental concentrations of chlorsulfuron in homes may result from spray drift, track-in, or from redistribution of residues brought home on the farmworker's clothing. Potential routes of exposure for children may include incidental ingestion and dermal contact with residues on turf, carpets/hard surfaces.

The chlorsulfuron assessment reflects the Agency's current approaches for completing residential exposure assessments based on the guidance provided in the OPPTS Harmonized Guidelines, *Series 875-Occupational and Residential Exposure Test Guidelines, Group B-Postapplication Exposure Monitoring Test Guidelines*, the *Draft: Standard Operating Procedures (SOPs) for Residential Exposure Assessment*, and the *Overview of Issues Related to the Standard Operating Procedures for Residential Exposure Assessment* presented at the September 1999 meeting of the FIFRA Scientific Advisory Panel (SAP). The Agency is, however, currently in the process of revising its guidance for completing these types of assessments. Further research into children's exposures resulting from agricultural uses of pesticides are being conducted by the Agency's Office of Research and Development through the STAR (Science to Achieve Results) grant program. The STAR program can be accessed at ***http://es.epa.gov/ncerqa/grants/*** Modifications to this assessment shall be incorporated as updated guidance becomes available. This will include expanding the scope of the residential exposure assessments by developing guidance for characterizing exposures from other sources not addressed such as from spray drift and exposures to farm worker children.

There is not likely to be a spray drift/track-in concern for chlorsulfuron since direct post application exposure from the registered and new use of chlorsulfuron on rangeland and pastures do not have calculated risks of concern (MOEs ≥ target of 300).

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

In examining aggregate exposure, FQPA directs EPA to take into account available information concerning exposures from pesticide residues in food and other exposures for which there is reliable information. These other exposures include drinking water and non-occupational exposures, e.g., to pesticides used in and around the home. Risk assessments for aggregate exposure consider both short-, intermediate- and long-term (chronic) exposure scenarios considering the toxic effects which would likely be seen for each exposure duration.

Chlorsulfuron is a food use chemical. Drinking Water Levels of Comparison (DWLOC) have been calculated for chlorsulfuron. There are residential (non-occupational) uses of chlorsulfuron; therefore, the considerations for aggregate exposure are those from food, drinking water and residential exposure.

5.1 Acute Aggregate Risk Assessment

An acute endpoint was not identified by the HIARC; therefore, no acute aggregate risk assessment is required.

5.2 Chronic Aggregate Risk Assessment

When drinking water concentrations are estimated using modeling as was the case for chlorsulfuron, Drinking Water Levels of Comparison are calculated (DWLOCs). DWLOCs represent the maximum contribution to the human diet, in μg/L, that may be attributed to residues of a pesticide in drinking water after dietary and residential exposure is subtracted from the cPAD. Since no chronic residential scenarios have been identified, chronic DWLOCs for chlorsulfuron were calculated based on residues in food alone. These are presented in Table 9. Comparisons are made between DWLOCs and the estimated concentrations (EECs) of chlorsulfuron in surface water generated with FIRST. If model estimates are less than the DWLOC, there is generally no drinking water concern. DWLOC calculations used the following equation and standard body weight and water consumption values, i.e., 70 kg/2L (adult male), 60 kg/2L (adult female) and 10 kg/1L (child).

Table 9. Chlorsulfuron Summary of Chronic DWLOC Calculations

Population Subgroup	cPAD (mg/kg/day)	Food Exposure (mg/kg/day)	Available Water Exposure (mg/kg/day)	DWLOC (ug/L)	Drinking Water EEC (ppb)
U.S. Population	0.02	0.001310	0.01869	654	41.3
Females 13-50 yrs	0.02	0.000857	0.01914	574	41.3
Children 1-6 yr	0.02	0.003869	0.01613	161	41.3
All Infants	0.02	0.001458	0.01854	185	41.3

Surface water EECs are from FIRST modeling;

$$\text{DWLOC} = \frac{\text{water exposure X body weight}}{\text{Liters of water X}10^{-3}} \text{ where water exposure = cPAD - food exposure}$$

Body weight = 70 kg for U.S. Population, 60 kg for females, 10 kg for infants and children
Liters of water = 2L for Adults and 1L for infants and children

Chronic DWLOCs. As shown in Table 9, comparison of the chronic DWLOCs with the environmental concentrations of chlorsulfuron estimated using conservative modeling show that drinking water concentrations are less than the DWLOCs for all populations. Consequently, there is no chronic aggregate concern for drinking water.

5.3 Short-term Aggregate Risk Assessment

Short-term DWLOCs were calculated based upon average food residues and residential handler exposure. Residential exposure considers postapplication exposure of adults and toddlers to treated lawns.

Table 10. Short-Term Aggregate Risk and DWLOC Calculations

Population	Short -Term Scenario								
	NOAEL mg/kg/day	Target MOE[1]	Max Exposure[1] mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure[2,3] mg/kg/day	Aggregate MOE (food and residential)[4]	Max Water Exposure[5] mg/kg/day	Drinking Water EEC[6] (μg/L)	Short-Term DWLOC[7] (μg/L)
Adult Male	75	300	0.25	0.001310	0.058	1265	0.19	41.3	6674
Adult Female	75	300	0.25	0.000857	0.058	1274	0.19	41.3	5734
Toddler	75	300	0.25	0.003869	0.10	722	0.15	41.3	1461

[1] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

[2] Residential Exposure = [Oral exposure (all routes)+ Dermal exposure + Inhalation Exposure]

[3] Toddler Residential Exposure = Dermal + Hand to Mouth + Object to Mouth + Soil Ingestion

[4] Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]

[5] Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

[6] The crop producing the highest level was used.

[7] DWLOC(μg/L) = $\frac{\text{[maximum water exposure (mg/kg/day) x body weight (kg)]}}{\text{[water consumption (L) x } 10^{-3} \text{ mg/}\mu\text{g]}}$

Short-term DWLOCs. As shown in Table 10, drinking water concentrations estimated using conservative modeling are below the short-term DWLOCs for chlorsulfuron. Consequently, there is no short-term exposure concern for drinking water even when using conservative drinking water estimates.

6.0 CUMULATIVE RISK

The Food Quality Protection Act (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this new use for chlorsulfuron because HED has not yet initiated a review to determine if there are any other chemical substances

that have a mechanism of toxicity common with that of chlorsulfuron. For purposes of this reregistration decision EPA has assumed that chlorsulfuron does not have a common mechanism of toxicity with other substances.

On this basis, the registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether chlorsulfuron shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for chlorsulfuron need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with chlorsulfuron, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment once the final guidance HED will use for conducting cumulative risk assessments is available.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on June 30, 2000 (65 FR 40644-40650) and is available from the OPP Website at: *http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-30/6049.pdf* In the draft guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed. The proposed guidance on cumulative risk assessment of pesticide chemicals that have a common mechanism of toxicity is expected to be finalized by the summer of 2002.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

7.0 OCCUPATIONAL EXPOSURE

Based on the proposed use patterns, short- and intermediate- term dermal and inhalation occupational exposure are expected. Based on the early season (applied at germination or actively growing) use patterns, chronic occupational exposure to chlorsulfuron is unlikely. No chemical specific data are available to assess potential exposure to pesticide handlers (i.e., mixer/loaders and applicators), therefore, the Pesticide Handlers Exposure Database (PHED, 1.1, 1998) is the basis of exposure calculations. Due to use pattern and crops with minimal worker tasks, no postapplication exposure is expected or assessed.

7.1 Handler Exposures & Risks

Occupational handler exposure risk from the proposed use on rangeland and pastures is calculated based on the equipment being used. Equipment-based risk calculations are

separated into scenarios according to the tasks, equipment and PHED. Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of this new use of chlorsulfuron. It is the policy of the HED to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available (HED ExpoSAC Policy 007). The maximum application rate listed on the proposed use was used for all calculations. The standard values for acreage were taken from the HED Exposure SAC Policy 9.1 effective Sept. 25, 2001.

Currently, HED recommends that the exposure and risk estimates for mixer/loaders and applicators of tractor drawn equipment remain separate unless specific chemical and/or crop information exists to warrant the combining of the two estimates. Therefore, scenarios applicable to mixing/loading and applying chlorsulfuron by groundboom were not included in the handler exposure assessment for the proposed uses. While HED realizes that each use could be mixed, loaded and applied by the same person, the studies in PHED do not monitor that type of product use. Combining of mixer/ loaders and applicator data from separate PHED scenarios is outside the scope of the database. For chlorsulfuron, the following PHED scenarios were used.

Mixer/Loaders: (M/L)

Scenario 1: Mixing and Loading Dry Flowable for Aerial Application (wheat, high acreage).
Scenario 2: Mixing and Loading Dry Flowable for Aerial Application (cereal grains only, low acreage).
Scenario 3: Mixing and Loading Dry Flowable for Groundboom Application (cereal grains).
Scenario 4: Mixing and Loading Dry Flowable for Groundboom Application (grass areas).
Scenario 5: Mixing and Loading Dry Flowable for High Pressure Handwand Application (grass areas).

Applicators (APP)

Scenario 6: Sprays by Aerial Application (wheat).
Scenario 7: Sprays by Aerial Application (cereal grains only).
Scenario 8: Sprays by Groundboom Application (cereal grains only).
Scenario 9: Sprays by Groundboom Application (grass areas).
Scenario 10: Sprays by High Pressure Handwand (cereal grains).
Scenario 11: Flagger for Aerial Application (cereal grains only)

The following assumptions were used in this assessment:

* Body weight of 70 kg, since the toxicological endpoint point is for the general population (not gender specific).
* Maximum rate per acre is used.
* 8 hour workday with a range of acres to account for varying equipment types and field size.
* Mixer and loaders of chemical are not also applying the chemical.
* Only baseline clothing scenario exposure risks were calculated since the MOEs for short-term exposures were well above the target MOE of 100. Not all registered labels contain the personal protective equipment requirements. Baseline clothing should be stated on each label.

The potential exposures and risks within the 11 identified exposure scenarios were assessed using the toxicological endpoints and uncertainty factors associated with the active ingredient. Table 11 provides short-term exposure risk calculations for handlers wearing baseline clothing, long sleeved shirt, long pants, socks and shoes. All route specific and combined MOEs are greater than the target MOE of 100 and therefore risks are not of concern (MOEs range between 1,000 and 71,000).

Table 11: Chlorsulfuron Handler Exposure: Baseline Clothing.*

Scenario	Acres /day	Application Rate lb ai/A	Dermal Unit mg/lb ai	Inhalation Unit μg/lb ai	Dermal Exposure[a] mg/day	Dermal Dose[b] mg/kg/day	Inhalation Exposure[c] mg/day	Inhalation Dose[d] mg/kg/day	MOE[e] Dermal	MOE[e] Inhalation	MOE[e] Combined[f]
Mixer/Loader											
1. Aerial Grain	1200	0.0625	0.066	0.77	5.0	0.071	0.058	0.00083	1100	91000	1000
2. Aerial: Grain	350		0.066	0.77	1.4	0.021	0.017	0.00024	3600	310000	3600
3. Broadcast: Grain	200		0.066	0.77	0.83	0.0118	0.0096	0.00014	6400	550000	6300
4. Broadcast: Grasses	80	0.14	0.066	0.77	0.74	0.0110	0.0086	0.00012	7100	6.1e+05	7000
5. HPHW (x100 gal)	10		0.066	0.77	0.09	0.00130	0.00110	1.5e-05	57000	4.9e+06	56000
Applicator											
6. Aerial Grain	1200	0.0625	0.0050	0.068	0.38	0.0054	0.005	7.3 e -05	14000	1.0 e+06	14000
7. Aerial Grain	350		0.0050	0.11	0.11	0.0016	0.002	2.1 e -05	48000	3.5 e+06	47000
8. Broadcast Grain	200		0.014	0.74	0.18	0.0025	0.0093	0.00013	30000	570000	28000
9. Broadcast Grasses	80	0.14	0.014	0.74	0.070	0.00100	0.0037	5.3e-05	75000	1.4e+06	71000
10. HPHW** (x100 gal)	10		1.8	79	1.13	0.016	0.049	0.00071	4700	110000	4500
11. Flagger Grain	350	0.0625	0.011	0.35	0.24	0.0034	0.0077	0.00011	22000	6.9e+05	21000

* Baseline clothing includes long sleeved shirt, long pants, socks and shoes. This table is generated with a spreadsheet program. The result of calculations are shown to 2 significant figures which may result in rounding differences.

** HPHW: High Pressure Handwand: spot treatments only (100*10 = 1000 gal use).

a Dermal Exposure (mg/day) = Acres/day *Application Rate (lb ai/A) * Dermal Unit (mg/lb ai).

b Dermal Dose (mg/kg/day) = [Dermal Exposure (mg/day) * Dermal Absorption (100% / 100%)] ÷ Body Weight (70 kg).

c Inhalation Exposure (mg/day) = Acres/day *Application Rate (lb ai/A) * Inhalation Unit (μg/lb ai) * Conversion (1mg/1000 μg).

d Inhalation Dose (mg/kg/day) = Inhalation Exposure (mg/day) *Inhalation Absorption (100% / 100%)÷ Body Weight (70 kg).

e (Inhalation or Dermal) MOEs (unitless) = NOAEL (75 mg/kg/day) ÷ Dose (Inhalation or Dermal). Target MOE = 100.

f Combined MOE (unitless) = $\frac{1}{\frac{1}{MOE_{dermal}} + \frac{1}{MOE_{Inhalation}}}$ Target Combined MOE = 100.

The potential exposure risk calculated for handlers had MOEs above the target value of 100, therefore were not of concern. No chemical specific monitoring study, market data or use closure memo was available when this assessment was written. Each scenario was

evaluated using PHED data and standard values according to HED practice and policy. The standard values and PHED data are selected to represent median to high end risk; therefore, the assessment was conservative.

The PHED data used to conduct the exposure risk calculations were of mixed quality and grade. Due to the data and lack of application information and market trends, whether this assessment represents an over or underestimate of risk is unclear. Long-sleeved shirt, long pants socks and shoes should be listed on the label. It should be noted, however, that the lowest handler MOE is 3X above the target MOE of 100.

7.2 Post-Application Exposures & Risks

Due to use pattern and crops with minimal worker tasks, no postapplication exposure was expected or assessed.

7.3 Incidents

A preliminary check of the Reference File System (REFs) on chlorsulfuron revealed some incidences. Some are registrant reports on incidents and all state that the contribution of chlorsulfuron to incidence is "unknown." A more thorough review of available sources on pesticide incidences is needed.

8.0 Data Needs/Label Requirements

8.1 Chemistry

* Develop a simpler enforcement analytical method or radiovalidate the existing method.
* Testing through the multiresidue methods

8.2 Toxicology

* Eye irritation
* Skin irritation study
* Dermal sensitization study
* 2-generation reproduction study,
* 21-day repeat dermal toxicity study,
* subchronic inhalation study.

8.3 Occupational/Residential Exposure

* The residential use as a spot treatment on turf reads, "a rate of 1.0 to 5.33 ounces per acre to cover 725 to 4000 sq.ft depending upon weed species." This wording should be rewritten to be equivalent to 0.25 lb ai/ A or 0.0057 lb ai/1000 sq ft.

References

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cc: F; Fort (RRB1), L. Taylor (RRB1), S. Hanley (RRB1)
RDI: W. Phang:RRB1:07/18/02

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