

**ASSESSMENT OF THE TOLERANCES
FOR SECTION 3 REGISTRATION OF
SHADEOUT™ (Rimsulfuron) ON TOMATOES**

**DEPARTMENT OF PESTICIDE REGULATION
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY**

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EXECUTIVE SUMMARY

A Section 3 registration is being requested for Shadeout™ which contains the herbicide, rimsulfuron. This registration is for a new use of rimsulfuron to control weeds in tomato fields. The proposed tolerance for rimsulfuron on tomatoes is 0.1 ppm.

The critical acute No-Observed-Effect Level (NOEL) was 500 mg/kg/day based on a ruffled fur and transient weight losses in rats after a single exposure and death in pregnant rabbits after 9 days of exposure. The critical NOEL for evaluating chronic exposure was 1.6 mg/kg/day based on increased liver enzymes and testicular degeneration in dogs exposed to rimsulfuron in the diet for 1 year. There does not appear to be any increased pre- or postnatal sensitivity to rimsulfuron based on two developmental toxicity study and one reproductive toxicity study. Therefore, no additional uncertainty factor, as required under the FQPA, is recommended. There was no evidence of oncogenicity in long-term studies with either rats or mice exposed to rimsulfuron in their diet. No information was available for review regarding potential endocrine effects of rimsulfuron.

The dietary exposure analysis utilized U.S. EPA established tolerances for all currently registered and proposed uses on commodities. The 95th percentile and the average exposure for each population subgroup were used in acute and chronic (annual) analysis, respectively. Based on the rapid degradation of rimsulfuron and its metabolites in water and soil, it is unlikely they would leach to groundwater. Therefore, no residues of rimsulfuron are anticipated in drinking water. Currently, there are no registered residential uses of rimsulfuron. No occupational exposure from aerial application of Shadeout™ is expected since the label states not to apply by air. Workers applying rimsulfuron to tomatoes were considered to be potentially exposed during ground mixing/loading and application activities.

A Margin of Exposure (MOE) of 100 is generally used as the benchmark for providing adequate protection of public health. This MOE takes into account the possibility that humans could be up to 10-fold more sensitive than the most sensitive test species on a dose per body weight basis and that the most sensitive human could be up to 10-fold more sensitive than an average person. The MOEs for potential acute and chronic dietary exposure were greater than 300,000 and 3,000, respectively. The highest potential chronic dietary exposure was approximately 3% of the U.S. EPA Reference Dose (RfD) for children 1-6 years old. The MOEs for potential acute and chronic occupational exposure were greater than 100,000 and 4,000, respectively. When dietary exposure was added to occupational exposure for workers, the MOEs for acute and chronic exposure were still greater than 90,000 and 3,000, respectively.

I. INTRODUCTION

A. Proposed Section 3 Use

A Section 3 registration is requested for the new product,, which contains 25% rimsulfuron (N-((4,6-dimethoxyypyrimidin-2-yl)aminocarbonyl)-3-(ethylsulfonyl)-2-pyridinesulfonamide). Rimsulfuron is a sulfonylurea herbicide currently registered for use to control broadleaf weeds and grasses. The proposed new use is on tomatoes. The registrant is E.I. du Pont de Nemours and Company. Shadeout™ should only be applied by ground and mixed with enough water to deliver 10 to 40 gallons of total spray per acre. The total application of Shadeout™ should not exceed 4 oz. product per acre per year (1 oz. rimsulfuron/acre/year). No more than 2 oz. product per acre should be applied preemergence or postemergence to a crop during the same growing season. The preharvest interval for tomatoes treated with Shadeout™ is 45 days.

B. Registration Status

There is currently only one other product containing rimsulfuron that is registered for use in California, Matrix. The concentration of rimsulfuron in this product is also 25%. The registrant for Matrix is also E.I. du Pont de Nemours and Company. Matrix is approved for use in California on potatoes. There is also a U.S.EPA tolerance for rimsulfuron on field corn. The tolerances for tomatoes, potatoes, and field corn were all used in dietary exposure assessment for rimsulfuron.

C. Scope

The Food Quality Protection Act of 1996 (FQPA) requires that a tolerance with an expiration date or an exemption from tolerance be established for the emergency use of a pesticide. The implementation of the FQPA is still in its early stages. USEPA is currently addressing some crucial issues specified by the FQPA. Because of the urgency to use this product on tomatoes, DPR has conducted a limited risk assessment which addresses the potential aggregate exposure of the general public to rimsulfuron through the diet, drinking water, and any residential use. This assessment addressed the potential health effects from dietary and occupational exposure to rimsulfuron from its proposed use on tomatoes. Since this is a Section 3 registration request, this assessment addressed both acute and chronic (annual) exposures.

II. HAZARD IDENTIFICATION

The identification of the potential human health hazard is based on the toxicological studies submitted for the registration of rimsulfuron.

A. Pharmacokinetics

When rats were administered 25 or 250 mg/kg of radiolabeled rimsulfuron by oral gavage, 60-70% and 20-30% of the radioactivity was excreted in the urine and feces, respectively (Hawkins, 1989). Most of the radioactivity was excreted within 48 hours. Dosing regimens in which the animals were predosed for 14 days or received a 10 times greater dose did not significantly change the excretion profile. Since rimsulfuron was not administered intravenously for comparison, the oral absorption was assumed to be 60% based on the lowest percentage excreted in the urine. Metabolism of the parent compound included deamidation, demethylation of the one of the oxymethyl groups on the pyrimidine ring and hydroxylation of the pyridine or pyrimidine rings. No data was available regarding dermal absorption; therefore, the dermal absorption was assumed to be 100%.

B . Acute Toxicity

A no-observed-effect level (NOEL) was not clearly established in any of the available toxicity studies for rimsulfuron. A limit test was conducted in which 5 rats/sex were administered rimsulfuron by oral gavage at 5000 mg/kg (Server, 1988). No deaths were observed and the only other possible adverse effects noted were ruffled fur the day after dosing and transient weight losses (~5% of previous days weight). A NOEL of 500 mg/kg could be estimated by dividing the lowest-observed-effect level (LOEL) by 10.

In a rat developmental toxicity study, a maternal NOEL of 2000 mg/kg/day was established based on reduced weight gain and food consumption at 6000 mg/kg/day during the exposure period (gestation days 7-16) (Alvarez, 1989a). All 25 rats at 6000 mg/kg/day also had tan feces which is probably due to unabsorbed test material in the feces. No developmental effects were seen. The reduced food consumption was first observed between gestation days 9 and 11. The reduced body weight gain was observed during gestation days 11 and 13. Although these effects are probably not due to a single exposure, the maternal NOEL was assumed to also be the acute NOEL.

In a rabbit developmental toxicity study, a maternal NOEL of 170 mg/kg/day was established based on one death on gestation day 25 at 500 mg/kg/day (Alvarez, 1989b). Rabbits were exposed to rimsulfuron on days 7-19 of gestation. Abortions and weakness were also seen at 500 mg/kg/day in two animals each, but not until after the exposure period. The only effects observed during exposure were decreased food consumption (days 13-16) and orange-stained cageboards. The orange-stained cageboards are probably due to excretion of the test article and/or metabolites since they were only observed during the exposure period. At 1500 mg/kg/day, 5 deaths, weakness and orange-stained cageboards were observed during exposure. Ten deaths and 3 abortions occurred after the end of the exposure period. Weakness and no or small feces were often seen a day or two before the deaths. All the animals that died, except one, had mucosal hemorrhages in the stomach. No adverse developmental effects were observed in this study with the possible exception of abortions. These occurred at 500 and 1500 mg/kg/day after exposure ended and may be related to maternal toxicity. Furthermore, there was no indication of fetotoxicity based on the lack of significant differences in the pre- and post-implantations losses and stillbirths. The one death and 2 abortions at 500 mg/kg/day should probably not be considered acute effects due to their late occurrence in the study. However, some deaths at 1500 mg/kg/day occurred earlier (gestation day 16 or exposure day 9) and, theoretically, could be the result of a single exposure. Therefore, the acute NOEL for this study was estimated to be 500 mg/kg based on the mortalities at 1500 mg/kg/day.

A critical NOEL of 500 mg/kg was selected for evaluating the potential health effects from acute exposure to rimsulfuron based on ruffled fur and transient weight losses in rats after a single exposure at 5000 mg/kg and deaths in pregnant rabbits after at least 9 days of exposure at 1500 mg/kg/day. The critical NOEL was adjusted for oral absorption (60%) when evaluating occupational exposure since occupational exposure was expressed as absorbed dosages. After correcting for absorption, the adjusted acute NOEL was 300 mg/kg. The unadjusted acute NOEL was used for evaluating dietary exposure because the oral absorption was assumed to be the same for laboratory animals and humans.

B. Chronic Toxicity

Numerous effects were observed in dogs administered rimsulfuron in the diet at 2500 ppm (M:81.8 mg/kg/day; F:86.5 mg/kg/day) and 10,000 ppm (M:342.4 mg/kg/day;F:358.5 mg/kg/day) for 1-year (Atkinson, 1991). Corneal opacity was observed at 10,000 ppm. The cholesterol and alkaline phosphatase values were significantly elevated in serum at 2500 and 10,000 ppm suggesting hepatotoxicity. An increase in urine volume and decrease in urine

osmolality and specific gravity were observed at 2500 ppm, but the differences were only statistically significant in the males at 10,000 ppm. The liver and kidney weights were also elevated at 2500 and 10,000 ppm. With microscopic examination, testicular degeneration characterized by a reduction in the diameter of seminiferous tubules and a reduction in the number or lack of germ cells was seen at 2500 and 10,000 ppm. Spermatid giant cells were also observed in the epididymis at 2500 and 10,000 ppm. In addition, tracheal hyperplasia and/or subacute inflammation were observed at 2500 and 10,000 ppm. This study was acceptable based on FIFRA guidelines. A critical NOEL of 50 ppm (M&F:1.6 mg/kg/day) was selected for evaluating the potential health effects from chronic exposure to rimsulfuron. As with the acute NOEL, the chronic NOEL was adjusted to 0.96 mg/kg/day for evaluating occupational exposure based on oral absorption (60%). The unadjusted chronic NOEL was used for evaluating dietary exposure because the oral absorption was assumed to be the same in laboratory animals and humans. U.S. EPA used the same study and NOEL with a standard uncertainty factor of 100 to derive an RfD of 0.016 mg/kg/day for rimsulfuron (U.S. EPA, 1997).

C. Pre- and Post-natal Sensitivity

Developmental toxicity studies in rats and rabbits and reproductive toxicity studies in rats were considered in assessing the potential for higher sensitivity in infants and children than adults. Both developmental toxicity studies and the one reproductive toxicity study were found acceptable to DPR based on the FIFRA guidelines. As discussed under the Acute Toxicity Section, the only possible adverse developmental effect was abortions which were observed in the rabbit developmental toxicity study at 500 and 1500 mg/kg/day (Alvarez, 1989b). Maternal deaths were also observed at 500 and 1500 mg/kg/day. It was unclear if these abortions were due to maternal toxicity or direct fetotoxicity. No significant differences in pre- and postimplantation losses were seen, suggesting that the abortions are probably due to maternal toxicity. Consequently, DPR identified the developmental NOEL as equal to or greater than 1500 mg/kg/day. In the Federal Register notice regarding rimsulfuron tolerances for field corn and potatoes (U.S. EPA, 1994a), U.S. EPA identified the developmental NOEL as 500 mg/kg/day since there were only 2 viable pups at 1500 mg/kg. Without more detailed information, the assumption was made that U.S. EPA considered the number of viable pups at 1500 mg/kg to be insufficient to determine a developmental NOEL. There was no comment in the Federal Register notice regarding the significance of the abortions. Regardless of which NOEL is selected for the developmental NOEL for this study, no possible adverse developmental effects were observed at dose levels below those which caused maternal toxicity (i.e., 500 mg/kg/day).

In the rat developmental toxicity study, a NOEL of 2000 mg/kg/day for maternal toxicity was lower than the NOEL of 6000 mg/kg/day (the highest dose tested) for developmental effects (Alvarez, 1989a). Maternal toxicity in rats included reduced weight gain and food consumption and altered fecal color. Based on these two studies, there does not appear to be any increased prenatal sensitivity to rimsulfuron.

In a reproductive study with rats, the postnatal NOEL was 3000 ppm (204 mg/kg/day) based on reduced pup weight gain (Mullin, 1990). DPR identified a maternal NOEL for adult rats for this study at 15,000 ppm (1,021 mg/kg/day), the highest dose tested. At the time of this study review, no paternal NOEL was established. However, based on significantly reduced body weights in the F₁ males, a paternal NOEL could be established at 3000 ppm (204 mg/kg/day). U.S. EPA identified a NOEL of 165 to 264 for both the reproductive and systemic effects for this study. The reproductive NOEL was based on a significant increase in small body size and a decrease in body weights of pups. The systemic NOEL was based on decreased body weights in F₁ males, decreased body weight gains in F₀ males and F₀ and F₁ females, and decreased food consumption in F₁ males. Both agencies agree in their evaluations in that body weight reductions in pups were seen at the same dose levels as the body weight reductions in adults, indicating there is no increased postnatal sensitivity to rimsulfuron. Therefore, an

additional safety factor for infants and children is not recommended in accordance with the FQPA.

D. Genotoxicity/Carcinogenicity

No evidence of genetic toxicity was found in any of the available tests for rimsulfuron (DPR, 1993). There was also no evidence of oncogenicity in the long-term studies conducted in rats and mice for rimsulfuron. According to the U.S. EPA Office of Pesticide Programs Reference Dose Tracking Report (U.S. EPA, 1997), rimsulfuron is classified as a Category E carcinogen (evidence of non-carcinogenicity for humans).

E. Endocrine Effects

No information was available for review regarding potential endocrine effects of rimsulfuron.

III. EXPOSURE ASSESSMENT

A. Dietary Exposure

Tolerances have been established (CFR, 1996) for rimsulfuron (N-((4,6-dimethoxyimidin-2-yl)aminocarbonyl)-3-(ethylsulfonyl)-2-pyridinesulfonamide) in or on field corn and potatoes at 0.1 ppm. The proposed tolerance for tomatoes is also 0.1 ppm.

Studies submitted regarding plant metabolism, analytical methods, and magnitude of residues for rimsulfuron in tomatoes were evaluated by DPR (Appendix A). No quantifiable residues were found (LOQ=0.05 ppm) in any of the samples including those treated at 5 times the maximum label application rate. Samples were collected 45 days after the final application to row-crop tomatoes and immediately after the final application to staked tomatoes.

No meat, milk or egg tolerances were proposed by the registrant because 1) no residues were found in the plant metabolism and magnitude of residue studies, 2) residues were minimal in animals when fed at exaggerated rates, and 3) tomatoes and its processed commodities are not fed to livestock. However, tomato pomace is fed to cattle in California (Appendix B). According to U.S. EPA's Pesticide Assessment Guidelines, Subdivision O (Residue Chemistry), tomato pomace may be fed to cattle up to 30% (U.S. EPA, 1994b). Regardless, in granting the tolerances for rimsulfuron on field corn and potatoes, U.S. EPA determined there is no reasonable expectation for residues in meat, milk, poultry or eggs (U.S. EPA, 1994a).

Acute Exposures

The results of the dietary exposure assessment are summarized in Table 1. Two sets of analysis are presented: the anticipated residues levels theoretical maximum residue concentration (TMRC) based on the tolerances for all commodities (currently registered and this proposed Section 3) and the TMRC for proposed Section 3 use on tomatoes only. The exposures were analyzed for 20 population subgroups based on U.S. geographic locations, ethnic origins, age and/or physiological status. Table 1 includes only the results for population subgroups of specific concern (e.g., children, women of child-bearing age) and those that exceeded the U.S. population exposure by 10% from either set of analysis. The dietary exposure assessment was conducted using TAS[®] software (TAS, 1996a&b) and the 3-year (1989-90, 1990-91, 1991-92) consumption data from the USDA Continuing Survey of Food Intakes by Individuals (CSFII) (USDA, 1989-91). Children 1-6 years old had the highest acute exposure based on the 95th percentile of the exposure distribution for consumption of tomatoes alone (0.855 µg/kg/day) or in combination with field corn and potatoes(1.334 µg/kg/day).

Table 1. Rimsulfuron Acute Dietary Exposure and the Corresponding Margin of Exposure (MOE)^a.

Population Subgroup	Current and Proposed Uses		Proposed Use on Tomatoes Only	
	Acute Dietary Exposure (µg/kg/day)	Acute Dietary MOE	Acute Dietary Exposure (µg/kg/day)	Acute Dietary MOE
U.S. Population (all)	0.748	670,000	0.479	> 1,000,000
Hispanics	0.822	590,000	0.602	830,000
Non-Hispanics Blacks	0.846	590,000	0.523	960,000
Infants, nursing	1.049	480,000	0.817	610,000
Infants, non-nursing	1.054	470,000	0.653	770,000
Children 1-6 yrs	1.334	370,000	0.855	580,000
Children 7-12 yrs	1.035	480,000	0.623	800,000
Females, 13+, pregnant	0.485	> 1,000,000	0.386	> 1,000,000
Females, 13+, nursing	0.573	870,000	0.378	> 1,000,000
Females 13-50 yrs	0.556	900,000	0.398	> 1,000,000
Males, 13-19 yrs	0.839	740,000	0.417	> 1,000,000
Seniors, 55+	0.477	> 1,000,000	0.343	> 1,000,000
Males/Females \$ 16 yrs	0.558	900,000	0.384	> 1,000,000

^a Residue set at the tolerance level (0.1 ppm) | for all commodities. The exposure represents the 95th percentile of the exposure distribution based on consumption. The margin of exposure (MOE) is the ratio of the NOEL over the exposure. The NOEL was 500 mg/kg/day based on ruffled fur and transient weight losses in rats after a single dose and death in pregnant rabbits exposed for 9 days.

The risk for human health effects is expressed as a margin of exposure (MOE). The MOE is the ratio of the NOEL from the experimental animal studies to the estimated human exposure dosage. The MOEs for acute dietary exposure are also summarized in Table 1. The acute MOEs are all greater than 300,000. Children 1-6 years old had the lowest MOE, 370,000, when exposure to residues on tomatoes, potatoes and field corn were combined.

Chronic Exposures

The long-term exposures were estimated based on tolerance levels for all commodities (current and proposed). Table 2 includes only the results for subgroups of specific concern (e.g., children, women of child-bearing age) and those exceeding the U.S. population exposure by 10%. Children 1-6 years old had the highest chronic dietary exposures from use of rimsulfuron on tomatoes, tomatoes, and field corn.

Table 2. Rimsulfuron Chronic Dietary Exposure and the Corresponding Margin of Exposure (MOE) and Percentage of the USEPA RfD

Population Subgroups	Chronic Dietary Exposure ^a (µg/kg/day)	Chronic Dietary MOE ^b	% U.S. EPA RfD ^c
U.S. Population	0.264	6,055	1.7%
Infants, nursing	0.095	16,921	0.6%
Infants, non-nursing	0.262	6,115	1.6%
Children 1-6 yrs	0.518	3,088	3.2%
Children 7-12 yrs	0.420	3,813	2.6%
Females, 13+, nursing	0.192	8,341	1.2%
Females, 13+, pregnant	0.227	7,036	1.4%
Males, 13-19 yrs	0.320	5,002	2.0%
Males/Females ≥ 16 yrs	0.186	8,619	1.2%
^a The anticipated residue levels were estimated based on the tolerances for field corn, potatoes, and tomatoes. ^b The MOE is the ratio of the NOEL over the exposure. The NOEL was 1.6 mg/kg/day based on liver enzyme changes and testicular degeneration in dogs. ^c The U.S. EPA RfD of 0.016 µg/kg/day was established from the NOEL of 1.6 mg/kg/day (increased liver and kidney weights and increased incidence of seminiferous tubule degeneration in dogs) and an uncertainty factor of 100.			

The risk for chronic dietary exposures is presented in Table 2, both in terms of MOE and the percentage of U.S. EPA RfD. The MOE was calculated using the NOEL of 1.6 mg/kg/day established by DPR based on liver enzyme changes and testicular degeneration in dogs. The U.S. EPA established the RfD of 0.016 mg/kg/day using the NOEL of 1.6 mg/kg/day based on increased liver and kidney weights and seminiferous tubule degeneration in dogs and applying an uncertainty factor of 100. Children 1-6 years old had the lowest MOE of 3,088 based on the DPR NOEL which represented 3.2% of the U.S. EPA RfD.

B. Aggregate Exposure

1. Drinking Water

The environmental fate data available for rimsulfuron has been reviewed previously (Appendices B and C). Although rimsulfuron and its environmental degradates, IN-70941 and IN-70942, are moderately mobile in soil, they degrade rapidly in both water and soil. Therefore, it is unlikely that they would leach to groundwater. The major pathways for dissipation of rimsulfuron appear to be hydrolysis and microbial metabolism.

2. Residential Exposure

Rimsulfuron is not currently registered for use on any residential non-food sites.

3. Occupational Exposure

Acute data for this formulation were provided to DPR. Based on the toxicity category, the proposed work clothing and personal protective equipment (PPE) appearing on the label are in compliance with the Worker Protection Standard (WPS). Acute data for the technical material are available. The proposed restricted entry interval (REI) of 4 hours appearing on the label is in compliance with the WPS. Information on assumptions used for estimation of potential exposure from occupational use is listed in Table 3.

Table 3. Occupational Exposure Assumptions for Rimsulfuron Use on Tomatoes

PARAMETER	ASSUMPTION
Pesticide Handlers Exposure Database (PHED), Version 1.1, Unit of Exposure From Best Available Surrogate Exposure Table (BASET, 4/10/96) Only ground applications allowed	Mixer/Loader, dry flowable, open system: Dermal = 66.2 µg/lb ai handled Inhalation =: 0.77µg/lb ai handled
	Applicator, ground, ground boom, open cab: Dermal = 14.0 µg/lb ai applied Inhalation = 0.7 µg/lb ai applied
Work Clothing and PPE	long pants, long-sleeve shirt, socks, shoes, waterproof gloves
Percent Absorption	Dermal: 100 % Inhalation: 100 %
Application Type	ground boom
Minimum Finish Spray	Ground: 10-40 gal/A
Maximum Application Rate	0.031 lb ai/A
Maximum Applications Per Year	2
Acres Treated/Day (Y. NG,BEAD)	Ground: 100 acres
Average Farm Size (1992 Ag Census)	Based on US Data 500 acres
Worker Weight	70 kg
Number of Farms Treated by PCO (Pest Control Operator)	Ground: 10 % Air: Not applicable

Exposure estimates were only calculated for workers involved in ground application since the label states not to apply Shadeout™ by air. The potential acute occupational exposure (Absorbed Daily Dose) for rimsulfuron use on tomatoes was 0.66 µg/kg/day for ground applicators and 2.99 µg/kg/day for ground mixer/loaders (Table 4). The potential chronic occupational exposures (Annual Average Daily Dose) were 0.05 µg/kg/day for ground applicators and 0.21 µg/kg/day for ground mixer/loaders.

Table 4. Occupational Exposure and Risk Assessment for Rimsulfuron Use On Tomatoes

Worker	Absorbed Daily Dosage ^a (µg/kg/day)	Annual Average Daily Dosage ^b (µg/kg/day)	Acute Occupational MOE ^c	Chronic Occupational MOE ^d
Ground Mixer/Loader	2.99	0.21	100,000	4,600
Ground Applicator	0.66	0.05	450,000	19,000

^a Absorbed Daily Dose (ADD) = PHED unit exposure x % absorption x application rate x acres treated/day) / kg body weight. (See Table 3.)

^b Average Annual Daily Dose (AADD) = ADD x number of days to treat average field x number applications/year x number of farms treated by PCO) 365 days/year.

^c Acute Occupational Exposure MOE = NOEL / ADD. After correcting for oral absorption (60%), the adjusted NOEL is 300 mg/kg/day based on ruffled fur and transient weight loss in rats after 1 dose and death in pregnant rabbits after 9 doses. MOEs are expressed to two significant figures.

^d Chronic Occupational Exposure MOE = NOEL / AADD. After correcting for oral absorption (60%), the adjusted NOEL = 0.96 mg/kg/day based in increased liver enzymes and testicular degeneration in dogs.

Since the occupational exposure represents an absorbed dose from dermal and inhalation exposure, the NOEL needed to be adjusted for oral absorption (60%) to calculate the MOE. The adjusted acute NOEL was 300 mg/kg/day. The MOEs for acute occupational exposure to rimsulfuron from use on tomatoes were 100,000 for ground mixer/loaders and 450,000 for ground applicators (Table 4). The adjusted chronic NOEL was 0.96 mg/kg/day. The MOEs for chronic occupational exposure from rimsulfuron use on tomatoes were 4,600 and 19,000 for ground mixer/loaders and ground applicators, respectively.

4. Combined Dietary and Occupational Exposure

For risk assessment purposes, the dietary exposure for males/females 16+ years was used to evaluate the combined dietary and occupational exposure for workers. Since the dietary exposure values represent an external dosage and the occupational exposure represents an internal dosage, the dietary exposure was corrected for oral absorption (60%). The adjusted acute and chronic dietary exposures for workers (16 yrs) were 0.33 and 0.11 µg/kg/day, respectively. The aggregate exposure for workers was calculated as the sum of their dietary and occupational exposure (Table 5). The potential acute aggregate exposure to rimsulfuron from use on tomatoes was 3.32 µg/kg/day for ground mixer/loaders and 0.99 µg/kg/day for ground applicators. The potential chronic aggregate exposure was 0.32 µg/kg/day and 0.16 µg/kg/day for ground mixer/loaders and ground applicators, respectively.

Since the aggregate exposure represents an absorbed dosage, the adjusted NOELs for acute and chronic effects (300 and 0.96 mg/kg/day, respectively) were also used for calculating MOEs. The MOEs for acute aggregate exposure to rimsulfuron were 90,000 for ground mixer/loaders and 300,000 for ground applicators (Table 5). The MOEs for chronic aggregate exposure were 3,000 and 6,000 for ground mixer/loaders and ground applicators, respectively.

C. Multiple Chemical (Cumulative) Exposure

Rimsulfuron is a sulfonyl urea herbicide. The herbicide action of this class of herbicides is due to its inhibition of acetolactate synthase which is an enzyme involved in biosynthesis of

Table 5. Aggregate Exposure and Risk Assessment for Rimsulfuron Use on Tomatoes

Worker	Acute Aggregate Exposure ^a (µg/kg/day)	Chronic Aggregate Exposure ^b (µg/kg/day)	Acute Aggregate MOE ^c	Chronic Aggregate MOE ^d
Ground Mixer/Loader	3.32	0.32	90,000	3,000
Ground Applicator	0.99	0.16	300,000	6,000

^a Acute aggregate exposure is the sum of the acute occupational and dietary exposure. After adjusting for oral absorption (60%), the acute dietary exposure for workers (\$ 16 yrs) is 0.33 µg/kg/day.

^b Chronic aggregate exposure is the sum of the chronic occupational and dietary exposure. After adjusting for oral absorption, the chronic dietary exposure for workers (\$ 16 yrs) is 0.11 µg/kg/day.

^c Acute aggregate margin of exposure (MOE) is the ratio of the acute NOEL to the acute aggregate exposure. After correcting for oral absorption, the adjusted acute NOEL is 300 mg/kg/day based on ruffled fur and transient weight loss in rats after a single dose and death in a pregnant rabbits after 9 doses. MOEs are expressed to two significant figures.

^d Chronic aggregate MOE is the ratio of the chronic NOEL to the chronic aggregate exposure. After correcting for oral absorption, the adjusted chronic NOEL is 0.96 µg/kg/day based on increased liver enzymes and testicular degeneration in dogs.

branched chain amino acids that is only found in plants (Brown, 1990). Consequently, this class of herbicides has relatively low toxicity. There are no data available to indicate that the toxic effects in mammals from rimsulfuron are cumulative with any other chemicals in this class or any other class.

IV. RISK APPRAISAL

Generally, an MOE of at least 100 is considered sufficiently protective of human health when the NOEL for an adverse systemic effect is derived from an animal study. The MOE of 100 allows for humans being 10 times more sensitive than animals and for the most sensitive human being 10 times more sensitive than the average human.

There does not appear to be a need for an additional uncertainty (safety) factor for the protection of infants and children in accordance with the FQPA. The NOELs for pre- and postnatal toxicity were equal to or greater than the NOELs for maternal or paternal toxicity in two developmental studies and one reproductive toxicity study.

The MOEs for acute and chronic dietary exposure were all greater than 300,000 and 3,000, respectively. The chronic dietary exposure was approximately 3% of the RfD in the potentially highest exposed population subgroup, children 1-6 years old. The actual MOEs are probably greater than those calculated in this assessment since the residues were set at the tolerance level. It is unlikely that anyone would consume all three commodities at the tolerance level on either an acute or chronic basis.

The MOEs for acute and chronic occupational exposure were greater than 100,000 and 4,000, respectively. After addition of dietary exposure, the MOEs for acute and chronic aggregate exposure for workers were still greater than 90,000 and 3,000, respectively.

V. CONCLUSIONS

The MOEs for potential acute dietary, occupational and combined exposure to rimsulfuron from the proposed use on tomatoes were all greater than 90,000. The MOEs for potential chronic dietary, occupational and combined exposure were all greater 3,000.

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- USDA, 1989-1991.** Food and Nutrient Intake of Individuals in the United States, 1 Day, 1989-1992. Continuing Survey of Food Intakes by Individuals, 1989-1992. U.S. Department of Agriculture, Agricultural Research Service.
- U.S. EPA, 1997.** Office of Pesticide Programs Reference Dose Tracking Report. United States Environmental Protection Agency, Washington, D.C. February 25, 1997.

APPENDIX A

Evaluation Report Regarding the Residue Chemistry for Shadeout™

**EVALUATION REPORT - PESTICIDE
Chemistry - Leffingwell**

Date: 30 September 1997

Product Name : DPX-E9636
I.D. No. : 167304-E
Applicant : E.I. du Pont de Nemours & Co., Agricultural Products Dept.
EPA Reg. No. : None Issued
Document No. : 51932-127 through -130
Active Ingredient : Rimsulfuron
Use : Herbicide
Registration Action : None
Area of Review : Residue Chemistry

Registration Specialist: F. Bundock

Data/Information Support Registration Data/Information Support Conditional
Registration
 Data/Information Do Not Support **No Registration Action Required**
Registration

Summary:

The Agricultural Products Department of E.I. du Pont de Nemours & Co. has submitted residue and metabolism data to support use of the subject active ingredient on tomatoes. Included are a study of the metabolism of rimsulfuron in tomatoes, a residue analytical method, a magnitude of the residues (MOR) of rimsulfuron in tomatoes, and a freezer storage stability of rimsulfuron residues in tomato fruit.

Discussion:

The metabolism of rimsulfuron in tomato plants was detailed (*Metabolism of ¹⁴C-DPX-E9636 Herbicide in Tomatoes*, du Pont report No. AMR 3520-95, DPR record No. 155041, volume No. 51932-128). Two studies were described, one conducted on field-grown tomato plants, and the other on potted plants grown in a greenhouse. Both studies utilized test material formulated into simulated 25% DF products using two versions of the active ingredient radiolabelled in separate rings; 0.25% of a surfactant-type adjuvant was added to the finished spray mixes, as well. In the field study, treatments were made at the 1.0 oz. a.i./A rate. The greenhouse study was conducted using exaggerated rates (2.5X, 5X, and 10X). No detectable radioactivity was found in the either immature or mature fruit from plants treated at any rate (harvested 30 to 60 days post treatment). Limits of detection for total radioactivity in fruit samples ranged from 0.003 to 0.013 ppm, depending on sample size, specific activity of the test material, and background radiation. Parent compound disappeared from tomato foliage in less than seven days (detectable only in the day-zero samples), and four metabolites were present at low levels (<0.5 ppm) for up to 60 days post treatment.

A residue analytical method was submitted (*Analytical Method for the quantitation of DPX-E9636 in Various Crops and Their Processed Fractions*, du Pont report No. AMR 3424-95, DPR record No. 155042, volume No. 51932-129). This is an upgraded version of AMR 1241-88, which has been evaluated previously (cf., memorandum of evaluation by M. Papathakis, dated 1 June 1995, for du Pont Matrix Herbicide, Tracking I.D. No. 150671-N). This method reports a limit of quantitation (LOQ) of 0.05 ppm and average recoveries from tomato fruit at 89 " 6%. No limit of detection was reported; however it was estimated to be 0.017 ppm. In addition, given the reported baseline noise level, the LOQ could have been set at 0.03 ppm and still have been ten times noise.

The report (*Magnitude of Residues of Rimsulfuron in Tomato Following Application of DPX-E9636 Experimental DF Herbicide at Maximum Use Rates and at Five Times Maximum Use Rates to Investigate the Need for Magnitude of Residue Data in Processed Fractions*, du Pont report No. AMR 3241-94, DPR record No. 155040, volume No. 51932-127) describes a series of seventeen MOR trials conducted in five states, of which twelve were done in California. Two crop and treatment scenarios were followed: 1) Staked (fresh market) tomatoes were treated with postemergence sprays directed to the row middles at a total rate of 1.0 (1X) and 2.0 (2X) oz. a.i./A; preharvest intervals (PHIs) ranged from zero to 21 days. 2) Row crop (processing) tomatoes were treated with postemergence broadcast sprays at a total rate of 1.0 and 2.0 oz. a.i./A; PHIs ranged from 40 to 89 days. One of the latter trials utilized 5.0 (5X) oz., instead of 2.0 oz. as the high rate, in order to determine the feasibility and necessity of conducting a tomato processing study. Samples were stored frozen after harvesting for periods between 8 and 157 days. All samples at all PHIs and treatment rates yielded undetectable residues (n LOQ) in mature tomatoes.

The stability of rimsulfuron residues in tomato matrices during cold storage (-20EC " 5EC) for up to six months (184 days) was detailed in du Pont report No. 3443-95 (*Storage Stability of DPX-E9636 in Frozen Analytical Samples of Tomato Fruit*, DPR record No. 155043, volume No. 51932-130). All the storage spikes were made at the 0.20 ppm level (4 times the LOQ), and held at - 20 EC. Samples were withdrawn for extraction and analysis at 0, 3, 14, 16, 21, 31, 62, and 184 days after spiking. Recoveries for the zero- through 21-day samples were very erratic, while the remaining three sample points were relatively consistent, but quite low (<70%). In fact, stability samples withdrawn during the period between 14 and 31 days suffered unacceptably low recoveries. All in all, this storage stability study appears to have had serious problems.

Conclusion:

Except for the freezer storage stability study, the submitted data are acceptable and could be used to support future registration of rimsulfuron-containing products for use on tomatoes. The residue and metabolism data show that tomato plants exposed to rimsulfuron at the post-transplant or post-emergent stage of growth produce mature fruit with no detectable residues of either the parent compound or known metabolites (as low as 0.003 ppm total residues). Therefore, these data support any proposed tolerance level greater than or equal to the 0.05 ppm

LOQ. Even though the freezer storage stability is inadequate to support the MOR data, the radiolabeled metabolism study provides sufficient evidence that the absence of detectable residues in the field trials is not due to degradation in storage. Residue data for tomato processing fractions would not be required, because no residues of rimsulfuron or its metabolites are likely to be present in any such fraction.

In addition, the residue data support labels that propose to use rimsulfuron at up to 2.0 oz. a.i./A., when the PHI is set at 40 days or more. The residue data from the trials on staked tomatoes do not necessarily support use on this variant of tomato culture where the PHI is proposed at less than 40 days, because the application pattern in these trials was that of a directed spray to the row middles, thus minimizing the possibility of the tomato plants being exposed to the herbicide spray. If future labels for this compound propose use on tomatoes at less than 40 days PHI, the use pattern must be restricted to a directed spray to the row middles, or new data supporting any other use pattern must be submitted.

John T. Leffingwell
Chief Chemist

APPENDIX B

Evaluation Report Regarding the Product Chemistry, Residue Chemistry and Environmental Fate Chemistry for Shadeout™

EVALUATION REPORT - PESTICIDE

Date: 1 October 1997

Chemistry - Leffingwell

Product Name : DuPont Shadeout Herbicide
I.D. No. : 168064
Applicant : E.I. du Pont de Nemours & Co., Agricultural Products Dept.
EPA Reg. No. : 352-556
Document No. : 51932-132, -133
Active Ingredient : Rimsulfuron
Use : Herbicide
Registration Action : Full Registration of Use on Tomatoes
Area of Review : Product Chemistry, Residue Chemistry, and Environmental Fate Chemistry

Registration Specialist: F. Bundock

Data/Information Support Registration Data/Information Support Conditional Registration
 Data/Information Do Not Support Registration No Registration Action Required

Summary:

The Agricultural Products Department of E.I. du Pont de Nemours & Co. has requested registration of the subject product for the control of listed weeds in tomatoes. To support this request, the applicant has submitted an application, a federal EPA Confidential Statement of Formula, dated 29 September 1995, for the identical product, DuPont Matrix Herbicide, (California Registration No. 352-556-AA), a proposed label, and a copy of the completed notification to the federal EPA for registration of the subject product as an alternate brand name for DuPont Matrix Herbicide. In addition, the applicant has submitted a copy of the petition for the establishment of a tolerance for rimsulfuron on tomatoes, and has cited supporting residue chemistry data on file with the Department (Tracking ID No. 167304-E, DPR Volume Nos. 51932-127 through -130).

Discussion:

Since du Pont Shadeout Herbicide is identical to du Pont Matrix Herbicide, evaluation of the pertinent product chemistry data has been completed (cf., memorandum of evaluation by M. Papathakis, dated 1 June 1995, Tracking I.D. No. 150671-N).

Reference is made to my Evaluation Report, dated 30 September 1997, regarding the residue chemistry data referenced above (attached), wherein I concluded that the data support a tolerance for the raw agricultural commodity, tomato fruit, at a level down to 0.05 ppm. In addition, the residue data support use rates on tomatoes up to a total of 2.0 oz. a.i./A, provided the preharvest interval (PHI) is set at 40 days or more.

The proposed label stipulates pre- or postemergence applications of 1.0 to 2.0 oz. product per acre (0.25 to 0.5 oz. a.i./A) per application by low-pressure, ground-boom spray equipment in 10 to 40 gallons of water. One pre-emergence plus one postemergence treatment may be applied. Banded application techniques may be employed, but require proportionately less spray mixture based on actual soil area treated. In addition, Shadeout may be applied by chemigation through center pivot, lateral move, solid set, or hand move irrigation systems, only. Other limitations include a 45-day PHI and a proscription against the use of aerial application or air-blast equipment. The label directions and restrictions are consistent with, and supported by the cited residue data.

The petition for the establishment of a tolerance for residues of rimsulfuron on tomatoes requests a level be set for tomatoes at 0.10 ppm. To support this request, the petition cites the same residue and metabolism studies referenced above. No food or feed additive tolerances are proposed for tomato processing fractions, because rimsulfuron residues are not expected to concentrate upon processing. No meat, milk or egg tolerances were proposed, because 1) rimsulfuron residues were not found in tomato fruit in MOR and metabolism studies, 2) rimsulfuron residues are minimal in animals even when fed at exaggerated rates, and 3) tomatoes and tomato processing fractions are not used in the diet of poultry, cattle, or swine. The last point is incorrect; cattle are fed tomato pomace in California (cf. the Memorandum of Evaluation, by M. Papathakis, dated 26 March 1997, Tracking I.D. Nos. 160478-NC, 160481-NC, and 160482-NC, regarding registration of azoxystrobin, and his memorandum, dated 16 May 1997, regarding the establishment of a California tolerance for azoxystrobin in tomato pomace). However, this point is of little consequence in this case for the reasons given in 1) and 2) above. A draft of the chemistry portions of a background document to be used by the federal Agency in generating the Federal Register Notice regarding the establishment of a tolerance for rimsulfuron on tomato fruit is attached.

Environmental fate data for rimsulfuron-containing products has been reviewed previously (cf., memorandum of evaluation by M. Papathakis, dated 1 June 1995, Tracking I.D. No. 150671-N). Although rimsulfuron and its environmental degradates, IN-70941 and IN-70942 are moderately mobile in soil, they are not sufficiently stable to pose any threat to groundwater. The major pathways for dissipation of rimsulfuron appear to be hydrolysis and microbial metabolism.

Conclusion:

The cited and submitted data support registration of the proposed label for duPont Shadeout Herbicide. The proposed tolerance of 0.10 ppm of rimsulfuron in or on tomato fruit is supported by the data, as well.

John T. Leffingwell
Chief Chemist

Attachment

APPENDIX C

**DPR Memorandum Regarding the Evaluation of Product Chemistry, Environmental Fate
Chemistry and Residue Chemistry for Matrix™**

Memorandum

To : Bob Rollins, Program Supervisor
Pesticide Evaluation

Date: June 1, 1995

Place: Sacramento

Phone: 324-3897

From : Department of Pesticide Regulation - Michael Papathakis
SPES (Chemistry)
Pesticide Evaluation

Subject: DUPONT MATRIX HERBICIDE

I.D. No. : 150671-N
EPA Reg. No.: 352-556
Doc. No. : 51932-001, -006 through -008, -10 through -014, -055,
-058,-061, -062, -064, -066 through -084, and -118.
Company : E.I. Du Pont De Nemours and Company, Inc.
A.I. : Rimsulfuron
Use : Herbicide

SUMMARY

E. I. Du Pont De Nemours and Company, Inc. has applied for a full California registration for Dupont Matrix Herbicide. This product contains the new active ingredient rimsulfuron and will be used for selective control of certain broadleaf weeds and grasses in potatoes. To support registration of the subject product, thirty three chemistry data volumes were submitted. These include product chemistry, environmental fate, and residue chemistry data.

Product Chemistry

Product chemistry data were submitted in data volumes 1 and 74 through 84. These data include physical and chemical properties of both the formulated product and technical rimsulfuron, descriptions of beginning materials and processes used to manufacture both Dupont Matrix Herbicide and technical rimsulfuron, and discussions of the impurities in technical rimsulfuron and their formation. They also include an analytical method which determines rimsulfuron in technical material, another method which determines rimsulfuron in either technical material or formulations, and additional methods which determine impurities in technical material. In addition, the submitted data include certified limits for the ingredients in the formulated product, certified limits or the active ingredient in

technical material, and the results of the analysis of eighteen batches of technical rimsulfuron for the percent of the active ingredient and impurities.

The chemical name for rimsulfuron is N-[(4,6-dimethoxy-pyrimidin-2-yl)aminocarbonyl]-3-(ethylsulfonyl)-2-pyridine-sulfonamide, the Du Pont code for this chemical is DPX-E9636, and its CAS Registry Number is 122931-48-0. In addition, the molecular formula of rimsulfuron is $\text{CB}_{14}\text{HB}_{17}\text{NB}_{5}\text{OB}_{7}\text{SB}_{2}$ and its molecular weight is 431.44.

Technical rimsulfuron is a white solid, has a paste-like odor, and its bulk density is 0.784 g/ml. Its melting point range is 176 to 178° C and its vapor pressure at 25° C was estimated as 1.1×10^{-8} torr. In addition, a slurry of technical rimsulfuron in HPLC water caused the pH to change from 5.89 to 4.32.

In a solubility study report (Vol. 83, Record No. 133970) that was reviewed and found acceptable, the water solubility of rimsulfuron is reported as 135 ppm at pH 5, 7300 ppm at pH 7, and 5560 ppm at pH 9. The reason rimsulfuron is more soluble at pH 7 than at pH 5 is that it is a weak acid with a pK_{aB} of approximately 4.0. The fact that this compound is a weak acid, however, does not explain why it is apparently less soluble at pH 9 than at pH 7. The lower apparent solubility at pH 9, instead, can be explained by the fact that rimsulfuron hydrolyzes at a more rapid rate at pH 9 than at pH 7.

In another solubility study (Vol. 82, Record No. 133967), the water solubilities of IN-70941 and IN-70942, two rimsulfuron degradation products, were determined as 740 ppm and 230 ppm, respectively.

In a partition coefficient study (Vol. 83, Record No. 133973) that was reviewed and found acceptable, rimsulfuron's KB_{owBS} were determined as 1.96 and 0.0345 at pH 5 and pH 7, respectively. Both values are relatively low indicating that rimsulfuron is not likely to bioconcentrate.

Rimsulfuron was stable when stored at room temperature for one year, was stable in solution in the presence of iron metal and ferric ions, and was stable two weeks when exposed to artificial sunlight.

In addition, it is not an oxidizing or reducing agent, does not explode when impacted, and is non-corrosive.

Technical rimsulfuron is manufactured using a 2-step batch process. In the first step, (4,6-dimethoxyprimidin-2-yl) carbamic acid, phenyl ester is produced by reacting phenyl chlorformate with 2-amino-4,6-dimethoxypyrimidine in the presence of N,N'-dimethylaniline all in dioxane at 25° C. In the final step, rimsulfuron is produced by reacting the product of the first step with 3-(ethyl-sulfonyl)-2-pyridinesulfonamide and lithium hydroxide in acetonitrile at 25° C, and when the reaction is complete, adding water and adjusting the pH to between 2 and 3 with sulfuric or hydrochloric acid. The acid converts the lithium salt of rimsulfuron to its acid form. Once formed, this active ingredient is precipitated out of the aqueous solution by the addition of few rimsulfuron seed crystals to the solution.

The analytical method used to determine rimsulfuron in the technical material involves reverse phase HPLC and the use of phenyl sulfone as an internal standard. The determination is accomplished with a 25 cm C-8 column, a 38% acetonitrile/62% pH 3.0 water (HB_{3B}POB_{4B}) mobile phase, a flow rate of 2 ml/minute, a column temperature of 40° C, a UV detector wavelength of 230 nm, and an injection volume of 10 microliters.

Data volume 74 (Record No. 133955) reported the results of the analysis of five batches of technical rimsulfuron, data volume 78 (Record No. 133964) reported the results of the analysis of ten batches of technical rimsulfuron, and data volume 83 (Record No. 133978) reported the results of the analysis of three batches of technical rimsulfuron. All batches were analyzed for the percent active ingredient using the method described above. The analytical results show that in every batch, the percent active was greater than 99%. Based on these analytical results the upper and lower certified limits for the active ingredient in technical rimsulfuron were established as 100% and 96%.

The batches of technical material were also analyzed for impurities. The results of the analyses were reported and reveal that technical rimsulfuron contains 12 impurities. The submitted data include explanations for the presence of each impurity in the technical material and analytical methods used to analyze them. The results also show that no impurity was detected in any batch at a level greater than 0.2%. Based on these analytical results, upper limits were established for each impurity and were reported in data volume 74 (Record No. 133955). These upper limits range from 0.3 to 0.5%.

Dupont Matrix Herbicide is a light-tan granular solid with no odor. Its density is 0.8 g/ml. It does not contain oxidizing or reducing agents, is not explosive, is not corrosive to the packaging material, and the pH of water containing a 1% dispersion of this product was 6.9. In a storage stability study, the subject product was stable for ten months at room temperature. In addition, it was stable in a 45° C oven for 3 weeks.

Matrix Herbicide, like technical rimsulfuron, is manufactured using a batch process. The process involves combining technical rimsulfuron with intentionally added inert ingredients in specified proportions, thorough blending of the mixture, grinding of the sample to an average particle size of 6-10 microns, and selecting of the proper particle size by using a cyclone separator and 60-mesh screens.

The EPA confidential statement of formula lists the upper and lower certified limits for the active ingredient in Matrix Herbicide as 27.5% and 25.0%. Twenty five percent is also the percentage of rimsulfuron listed on the subject product label.

Environmental Fate

Environmental fate data for rimsulfuron were submitted in volumes 6 through 8 and volumes 58, 61, 62, 64, and 66 through 73. These volumes include study reports submitted to satisfy all AB 2021 requirements. In addition, they include a report of a confined accumulation study on rotational crops, an aerobic aquatic metabolism study report, an analytical method for the determination of rimsulfuron in water, an analytical method for the determination of rimsulfuron in soil, a report of a study in which the photodegradation of a rimsulfuron degradate was examined, and a soil TLC study report.

A single hydrolysis study report (Vol. 6, Record No. 116353) was submitted, reviewed and found acceptable. It describes a study in which the hydrolysis of both (pyrimidine-2-P¹⁴C)-rimsulfuron and (pyridine-2-P¹⁴C)-rimsulfuron was examined in sterile pH 5, pH 7, and pH 9 buffered aqueous solutions at 25° C. All samples were treated at a concentration of 25 ppm.

The study results demonstrate that this compound degrades at a moderately rapid rate at pH 5 and pH 7 and at an even faster rate at pH 9. The half-life of the pyrimidine labeled material was 4.7 days at pH 5, 7.3 days at pH 7, and only 4.2 hours at pH 9. The half-life of the pyridine labeled material was 4.5 days at pH 5, 7.1 days at pH 7, and 10.9 hours at pH 9. The study results also demonstrate that after 30 days at pH 5, approximately 72% of the applied material had been converted to a compound designated IN-70941 and approximately 13 percent had been converted to IN-70942. They showed that after 30 days at pH 7, greater than 80% of the applied material was converted to IN-70942. And they showed that after 1 day at pH 9 most of the applied material had been converted to IN-70942. These two degradates are formed by contraction of the sulfonyleurea bridge of the parent compound. Their structures and chemical names are included in the attachment at the end of this memo.

A report of a study that examined the photodegradation of both (pyrimidine-2- $P^{14}C$)-rimsulfuron and (pyridine-2- $P^{14}C$)-rimsulfuron in water (Vol. 68, Record No. 133937) was submitted, reviewed, and found acceptable. In the study, the degradation rates of the two test materials were determined at pH 5, pH 7, and pH 9 under natural sunlight and in the dark. In addition, the degradation products were identified and quantified in the pH 7 samples. All samples were treated at a concentration of 25 ppm.

The results of the study show that exposure to sunlight does not significantly affect the degradation rate of rimsulfuron in water. Although exposure to sunlight seems to have had some effect on the degradation rate of this compound in the pH 5 buffered solution ($t_{B_{1/2B}}$ of 1.1 days in the sunlight vs 4.7 days in the dark), the degradation rates in the pH 7 and pH 9 solutions were no faster in the sunlight than they were in the dark. Conversely, the results of the pH 7 study, show that sunlight does significantly affect the degradation rate of the rimsulfuron degradate IN-70942 in water. In the dark samples taken at the final sampling interval (day 21), 75.4 percent of the pyridine labeled material and 76.4 percent of the pyrimidine labeled material was identified as IN-70942. On the other hand, in the irradiated samples taken on day 21, only 9.8 percent of the pyridine labeled material and 6.9 percent of the pyrimidine labeled material was identified as IN-70942. The pH 7 results also show that the samples exposed to light contained five polar degradates not seen in the samples kept in the dark.

A supplemental aqueous photolysis study report titled "Photodegradation of IN-70942 in pH 7 Buffer Solution" (Vol. 64, Record No. 133932) was also submitted. In this study, the degradation rate of IN-70942 was determined both under simulated sunlight (Xenon Arc Lamp) and in the dark. The results of this study support the results of the previous study. They show an estimated half-life of 26.8 hours in the artificial sunlight. At the same time, they show that IN-70942 is stable in the dark.

A single soil photolysis study report (Vol. 69, Record No. 133938) was submitted, reviewed, and found acceptable. It describes a study in which the photodegradation of both (pyrimidine-2- $P^{14}C$)-rimsulfuron and (pyridine-2- $P^{14}C$)-rimsulfuron was examined on a Sassafras sandy loam soil using natural sunlight. In the study, the soil was treated at a rate equivalent to 0.73 oz a.i./acre, about twice the maximum label use rate of 0.375 oz a.i./acre. The results of the study show that rimsulfuron degrades in the irradiated soil at approximately the same rate as it does in the dark controls. The estimated half-lives in both the irradiated samples and the dark controls were between 11 and 12 days.

A single aerobic soil metabolism study report (Vol. 7, Record No. 116354) was submitted, reviewed, and found acceptable. It describes a study in which the aerobic metabolism of both (pyrimidine-2- $P^{14}C$)-rimsulfuron and (pyridine-2- $P^{14}C$)-rimsulfuron was examined in the Sassafras sandy loam soil. In the study, all soil samples were treated with test material at the rate of 0.10 ppm, which is approximately 3.2 times the maximum label use rate. The duration of the study was one year.

The results of the aerobic study show that both labeled compounds degraded rapidly in soil ($t_{B_{1/2B}}$ of 21.3 days for both labels). In addition, the analytical results identify IN-70941 and IN-70942 as the major degradation products in the study. After twelve months, approximately 32% of the applied material was in the form of IN-70941 and approximately 22% of the material was in the form of IN-70942. As in the hydrolysis study, these degradates were formed by contraction of the sulfonylurea bridge of the parent compound. The structures and chemical names for IN-70941 and IN-70942 can be found in the attachment at the end of this memo.

A single aerobic aquatic metabolism study report (Vol. 70, Record No. 133950) was submitted. This study was conducted in Ontario,

Canada to satisfy Canadian registration requirements. In the study, the aerobic metabolism of both (pyrimidine-2-P¹⁴P)-rimsulfuron and (pyridine-2-P¹⁴P)-rimsulfuron was measured in 25° C sterile pond water, in 5° C sterile pond water exposed to a fluorescent light 16 hours per day, in 25° C non-sterile pond water, and in 5° C non-sterile water exposed to fluorescent light 16 hours per day. The analytical results show that the rimsulfuron half-lives were approximately 1 day in the 25° C sterile pond water, were approximately 2 days in the 25° C non-sterile pond water, averaged 71 days in the 5° C sterile pond water, and averaged 54 days in the 5° C non-sterile pond water. In addition, IN-70941 and IN-70942 were identified as the major degradation products in the study.

A single anaerobic soil metabolism study report (Vol. 71, Record No. 133951) was submitted, reviewed, and found acceptable. It describes a study in which the anaerobic metabolism of both (pyrimidine-2-P¹⁴P)-rimsulfuron and (pyridine-2-P¹⁴P)-rimsulfuron was examined in the Sassafras sandy loam soil. In the study, all samples were treated at the rate of 0.1 ppm. In addition, the study included a ten day aerobic phase and a sixty day anaerobic phase, sampling took place on day 0 and day 10 of the aerobic phase and day 5, 10, 15, 28, and 60 of the anaerobic phase, and samples were analyzed by HPLC and TLC.

The analytical results show that rimsulfuron degraded at a rapid rate in the anaerobic soil. The half-life of the pyrimidine labeled compound was 18.1 days and half-life of the pyridine labeled compound was 17.9 days. As in the aerobic study, the major metabolic pathway is a bridge-contraction reaction yielding IN-70941 and IN-70942.

A single batch equilibrium study report (Vol. 66, Record No. 133935) was submitted, reviewed, and found acceptable. The study was conducted with four soils, two sandy loams, a clay loam, and a silt loam. In the study, adsorption coefficients (K_{dB}) were estimated by linear regression analysis as 0.23 and 0.32 for the sandy loams, 1.36 for the clay loam, and 1.57 for the silt loam. Using these values, I estimated K_{OCB} values of 19.8 and 58.2 for the two sandy loams, 57.1 for the clay loam, and 66.0 for the silt loam. These K_{OCB} values indicate that rimsulfuron was only weakly to moderately adsorbed to the study soils.

An additional study report titled "Soil Mobility of DPX-E9636 and Its Soil Degradates by Soil TLC" (Vol. 67, Record No. 133936)

describes a study which determined the relative mobilities of rimsulfuron and its primary degradates IN-70941 and IN-70942 in the four soils of the batch equilibrium study. The results of the study show rimsulfuron to be mobile in all four soils. The results also show that, in every soil, both degradation products were less mobile than rimsulfuron and that the mobilities of the two degradates ranged from immobile to mobile in these soils.

Two terrestrial field dissipation study reports were submitted to satisfy AB 2021 requirements. Both were reviewed and found acceptable. The first (Vol. 72, Record No. 133952) describes studies conducted at sites in Mississippi, California, and Illinois and the second (Vol. 73, Record No. 133953) describes a study conducted at a site in Delaware. The test materials used in these studies were formulations similar to Matrix containing (pyridine-2- $P^{14}C$)-rimsulfuron and (pyrimidine-2- $P^{14}C$)-rimsulfuron. At each site, 22 open ended stainless steel cylinders (4" in diameter X 15") were driven into the soil such that one inch of each remained above ground. Next, the soil surface inside all 22 cylinders was treated with test material (eleven with pyridine labeled material and eleven with pyrimidine labeled material). The application rate at each of the sites was approximately 1.0 oz./acre, which is approximately 2.7 times the maximum label rate.

In the first study, two cylinders, one of each label, were harvested at eleven sampling times, day 0, 1, 3, 7, 14, and month 1, 2, 4, 8, 12, and 18. After a cylinder was harvested, it was capped at both ends, placed in a cloth bag, and labeled. Subsequently, a soil core (1" in diameter X 2 ft deep) was taken beneath each cylinder and was divided into two 1 ft segments. The cylinders and soil segments were placed in dry ice and shipped to the laboratory for analysis. The Delaware study protocol was the same as that in the first study with the following exceptions: Cylinders were harvested at ten sampling times instead of eleven, day 0, 1, 3, 7, 14, and month 1, 2, 4, 8, 12. And the additional soil cores were only taken at months 8 and 12.

At the laboratory, the soil in the cylinders was separated into four segments, 0-3 in., 3-6 in., 6-9 in., and 9-14 in., and aliquots of each segment were analyzed by combustion and LSC for radioactivity. Those containing greater than 0.01 ppm radioactivity were later analyzed using a reverse phase HPLC method to determine the concentration of parent rimsulfuron as well as identify and quantify the rimsulfuron degradates in the sample.

The analytical results of the two studies indicate that rimsulfuron degraded at a rapid rate at all four sites. In the two reports, the results were analyzed by linear regression and the following rimsulfuron half-lives were estimated: 7.9 to 9.6 days at the Mississippi site, 8.0 to 8.2 days at the California site, 15.9 to 17.7 days at the Illinois site, and 5.4 to 5.9 days at the Delaware site. The results also indicate that rimsulfuron and its degradates are not likely to leach in soil. At the four sites, almost all of the applied radioactivity was detected in the top 3" of soil and no radioactivity was detected below the 3 to 6" depth at any sampling interval. They also indicate that IN-70941 and IN-70942 were the major degradates at the three sites of the first study and IN-70941 was the major degradate at the Delaware site.

To support the rotational crop guidelines on the subject product label, the registrant submitted a confined accumulation study report (Vol. No. 8, Record No. 116355). The report describes a greenhouse study in which a Sassafras sandy loam soil (contained in pots) was treated with (pyrimidine-2- $P^{14}C$)-rimsulfuron and (pyridine-2- $P^{14}C$)-rimsulfuron at a rate equivalent to 0.72 oz. a.i. acre, approximately twice the maximum label rate of 0.375 oz. a.i./acre. The treated soil was then aged aerobically for either 30 days, 120 days, or 10 months and rotational crops were planted in the pots at the end of the aging period.

Soybeans, wheat, sugarbeets, and lettuce were planted in the soil aged 30 days. Soybeans, wheat, sugarbeets, lettuce, and sunflowers were planted in the soil aged 120 days. And soybeans, wheat, sunflowers, and sorghum were planted in the soil aged 10 months. Crops were grown to maturity. They were then harvested, divided into the raw agricultural commodities, and analyzed for $P^{14}C$ -residues. The commodities analyzed were lettuce, soybean beans and straw, wheat grain and straw, sugarbeet leaves and beets, sunflower seeds and leaves, and sorghum grain and straw.

The analytical results show that the soybean straw of the 30-day and 120-day aging periods and the wheat straw of all three aging periods were the only commodities in the study containing $P^{14}C$ -residues above the detection limit of 0.05 ppm. None of the detected residues, however, was parent rimsulfuron. In addition, the results indicate that if soil had been treated at the maximum label rate, only wheat straw of the 30-day aging period would have contained rimsulfuron residues significantly higher than the detection limit.

These data, therefore, support the guideline for wheat which requires a four month interval between an application and planting and the guideline for soybeans which requires a 10 month interval between an application and planting. The data also support all the other rotational crop guidelines on the label except one. The one not supported is the guideline for tomatoes, which allows the planting of that commodity one month after an application of Matrix. Before the tomato guideline can be approved, the registrant must submit supporting data.

Finally, two analytical methods were submitted. The first (Vol. 58, Record No. 133919) is used to determine rimsulfuron residues in water. This method involves extraction from water with a C-18 cartridge and analysis of the sample using HPLC. The HPLC conditions for this method include a C-18 analytical column, a mobile phase consisting of 15% acetonitrile/85% aqueous buffer (pH 7.5) containing an ion-pair reagent, and a U.V. detector at 240 nm. The method can be used to quantify residues as low as 1.0 ppb and the mean recovery at the 1.0 ppb level was 88%.

The second method (Vol. 61, Record No. 133925) is used to determine rimsulfuron in soil. This method involves extraction of the active ingredient from soil with a 1:1 mixture of acetonitrile and methylene chloride, cleanup of the sample with a phenyl HPLC column, and finally analysis of the sample using HPLC. The HPLC conditions for this method include RB_{XB}-C8 column, a mobile phase consisting of 10% methanol/90% aqueous buffer (pH 7.5), and a U.V. detector at 254 nm. The method can be used to quantify residues as low as 0.2 ppb and the mean recovery at the 0.2 ppb level was 86.5%. Based on the recovery data, both methods appear to be adequate for enforcement purposes.

Residue Chemistry

Residue Chemistry data were submitted in volumes 10 through 14, 55, and 118. These data include a plant metabolism study report, a report that describes six residue trials conducted in 1990, another that describes eight additional residue trials also conducted in 1990, a processing study report, an analytical method used to determine rimsulfuron residues in potato samples, and two freezer storage stability study reports.

A single potato plant metabolism study report (Vol. 10, Record No. 116358) was submitted. It describes a greenhouse study in which

potatoes (planted in pots) were treated with (pyrimidine-2- $P^{14}C$)-rimsulfuron and (pyridine-2- $P^{14}C$)-rimsulfuron. All potato plants were treated at an early postemergent stage and half of them were treated again 16 days later. The radiolabeled test materials were applied to the foliage in pH 7 buffered solutions (similar to Matrix) and the rate of all applications was 1.0 oz. a.i./acre, more than twice the maximum label rate.

Whole potato plants were sampled on the day of the first application, as well as on days 8, 14 and 82 (harvest day) after that application. They were also sampled on the day of the second application as well as on days 7, 14, and 66 (harvest day) after the second treatment. The plants were analyzed within hours of harvest. Whenever tubers were present, they were removed from the foliage and analyzed separately. Combustion analysis was used to determine the total radioactive residues in every sample and TLC and HPLC were used to characterize any quantifiable residues.

The analytical results show that the total radioactive residues in all potato tubers at harvest were below the quantitation limit of 0.02 ppm. They also show that the foliage of the treated potato plants contained quantifiable radioactive residues. These residues were characterized as parent rimsulfuron, IN-70941, IN-70942, as well as several other polar and non-polar compounds. The results, therefore, indicate that rimsulfuron applied to potato plants does not translocate to the tubers and that if Matrix Herbicide is applied to potato plants according to the use directions on the label, no residues above the detection limit of 0.05 ppm are expected on the potato tubers.

Two residue study reports were also submitted. The first (Vol. 11, Record No. 116360) describes six residue trials conducted in the southern United States (three in Florida, two in California, and one in Texas) and the second (Vol. 12, Record No. 116362) describes eight trials conducted in the northern United States (two in Idaho, and one each in Maine, Wisconsin, Colorado, N. Dakota, N. Carolina, and California). In both studies, each site consisted of two treatment plots and one control plot and every site was treated with Matrix Herbicide. The two reports were submitted to show the Department that the use of the subject product (in California) according to the use directions on the label will result in no rimsulfuron residues above the 0.1 ppm tolerance established by U.S. EPA. The use directions include a maximum application rate of 0.375 oz. a.i./acre, a maximum seasonal rate of 0.5 oz. a.i./acre, a 14 to

28 day interval between applications, and a 60 day pre-harvest interval.

The two reports do support the use directions on the subject product label for the following reasons: (1) The application rates at all sites were higher than the maximum application rate on the label. At every site, one plot was treated at 0.5 oz. a.i./acre and another was treated at 1.0 oz. a.i./acre. (2) All sites of the second study recieved two applications and the interval between applications were approximately 14 days, the minimum allowed according to the use directions. (3) At all sites in both studies, the preharvest interval ranged between 30 and 50 days, less than the 60-day preharvest interval on the label. (4) An analytical method titled "Analytical Method For the Quantitation of DPX-E9636 in Corn (Forage and Grain)" (Vol. 14, Record No. 116366), which gave average recoveries of 84% was used to analyze samples in both studies. (5) The analytical data show that no potato sample in either study contained a detectable rimsulfuron residue. The detection limit for the analysis was 0.05 ppm.

The analytical method used in the residue studies involves extraction of the samples with an aqueous phosphate buffer (pH 7.5) and the use of an homogenizer, cleanup of samples using a Zorbax Phenyl column and 44% methanol, pH 3.5 mobile phase, and analysis of the samples using a Zorbax RB_{XB} column, a 22% methanol, pH 6.5 mobile phase, and a U.V. wavelength of 254 nm. An additional residue study report (Vol. 13, Record No. 116364) was submitted. It describes a study in which potatoes treated with DPX-E9636 at a rate of 7.0 oz. a.i./acre were processed and the processed fractions were analyzed. No residues, however, were detected on any of the potatoes treated at this rate and consequently, none were detected in any potato processed fraction. This data, therefore, indicates that no detectable rimsulfuron residues are expected in any processed fraction from potatoes treated with Matrix Herbicide according to the label use directions.

Two storage stability studies were also submitted to support the submitted residue data. The first (Vol. 55, Record No. 133915) describes a study in which potato samples were fortified with 0.2 ppm rimsulfuron, stored up to two years at -20° C, and periodically analyzed to determine the stability of rimsulfuron under these storage conditions. The analytical results show that rimsulfuron was stable two years at -20° C. This data supports the analytical data of the two potato residues studies. In those studies, all

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samples were stored at -20° C and none was stored longer than 7 months.

The second report (Vol. 118, Record No. 134977) describes a study in which samples of potato processed fractions were fortified with 0.2 ppm rimsulfuron, stored up to six months at -20° C, and periodically analyzed to determine the stability of rimsulfuron under these storage conditions. The analytical results show that rimsulfuron was stable six months at -20° C. This data supports the analytical data of the processing study. In that study, all samples were stored at -20° C and none was stored longer than 5 months.

CONCLUSION

All product chemistry and residue chemistry data requirements have been satisfied. In addition, all required environmental fate data but one have been submitted. The only one not submitted was data supporting the tomato rotational crop guideline, which allows tomatoes to be planted in a field one month after it has been treated with Matrix Herbicide. Therefore, the department should recommend registration of the subject product with the following condition: The registrant must submit data supporting the tomato rotational crop guideline within one year.

The submitted data characterize rimsulfuron as a compound which is mobile in soil but degrades rapidly in both water and soil, and therefore, is not likely to leach to groundwater. This chemical also has low K_{ow} values which suggests that it will not bioconcentrate. Finally, the submitted residue data indicate that applications of Matrix Herbicide to potato plants will not result in any rimsulfuron residue above the 0.1 ppm tolerance established by U.S. EPA.

RECOMMENDATION

Register the subject product with the following condition: The registrant must submit data supporting the tomato rotational crop guideline, which allows tomatoes to be planted in a field one month after it has been treated with Matrix Herbicide. The registrant has one year to submit this data.

cc: Herota
Bundock