CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
HUMAN HEALTH ASSESSMENT BRANCH

SUMMARY OF TOXICOLOGY DATA
RIMSULFURON

Chemical Code # 3835, Document Processing Number (DPN) # 51932
SB 950 # not applicable (new active ingredient)
Original date: 5/27/93
Revised date: Nov. 5, 2015

DATA GAP STATUS

Chronic toxicity, rat:	No data gap; no adverse effect
Chronic toxicity, dog:	No data gap; possible adverse effect
Oncogenicity, rat:	No data gap; no adverse effect
Oncogenicity, mouse:	No data gap; possible adverse effect
Reproduction, rat:	No data gap; no adverse effect
Developmental toxicity, rat:	No data gap; no adverse effect
Developmental toxicity, rabbit:	No data gap; no adverse effect
Gene mutation:	No data gap; no adverse effect
Chromosome effects:	No data gap; no adverse effect
DNA damage:	No data gap; no adverse effect
Neurotoxicity:	Hen neurotoxicity study not required

Toxicology one-liners are attached.

All record numbers for the above study types through 286627 (Document No. 51932-0170) were examined. This includes all relevant studies indexed by DPR as of 10/27/15.

In the 1-liners below:
indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.

File name: t20151105
Revised by Name, Date Aldous, 11/5/2015

NOTE: The following symbols may be used in the Table of Contents which follows:
** = data adequately address FIFRA requirement
† = study(ies) flagged as "possible adverse effect"
(N/A) = study type not currently required

This record contains summaries of studies. Individual worksheets may be useful for detailed assessment.

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METABOLISM AND PHARMACOKINETICS **

** 51932-119; 137687; "The Absorption and Disposition of [^{14}C]-DPX-E9636 in the Rat," (Hawkins, D.R., *et al*.; Dept. of Chemical Metabolism and Radiosynthesis, Huntingdon Research Centre, Ltd., Cambridgeshire, England; HRC Report No. HRC/DPT 190/891138, 12/14/89); [^{14}C-pyridine]DPX-E9636, [^{14}C -pyrimidine]DPX-E9636 (spec. act.: 50 mCi/mg, radiochemical purity > 97%); Dosing-(all dosing by gavage) Group A: 5 animals/sex, [^{14}C-pyridine] DPX-3936, 25 mg/kg, single dose; Group B: 7 animals/sex, [^{14}C -pyridine]DPX-3936, pretreatment with non-radiolabeled DPX-E9636 at 25 mg/kg/day for 14 days before treating with a single dose of radiolabeled DPX-9636; Group C: 5 animals/sex, [^{14}C -pyridine]DPX-3936, 250 mg/kg, single dose; Group D: 5 animals/sex, [^{14}C -pyrimidine]DPX-3696, 250 mg/kg, single dose; Results: radiolabeled compound largely excreted unmetabolized (50 to 60%) within the first 24 hours after dosing; by 72 hours post dose, 60 to 70% of radiolabel excreted in urine, additional 20 to 30% isolated in the feces; different dosing regimens did not change the excretion profile; little radiolabel sequestered in tissues after 72 hours; metabolism of parent compound included de-amidation, demethylation of the one of the oxymethyl groups on the pyrimidine ring and hydroxylation of the pyridine or pyrimidine rings; Study acceptable. (Moore, 7/28/95)

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat **

51932-038; 121137; Acute oral toxicity; 811; Rat; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; project #757-88; 11/29/88; DPX-E9636-22 technical; 5000 mg/kg administered by gavage; 5M/5F; no deaths; ruffled fur was observed in 1 male and 1 female 1 day after dosing; all animals gained weight during the post dosing period, though some females experienced sporadic weight loss (up to 5% of the previous days weight); terminal necropsies were negative; LD_{50}(M/F) > 5000 mg/kg; Toxicity Category IV; **Acceptable. (Rubin, 3/4/93)

Acute dermal toxicity

**51932-039; 121139; Acute dermal toxicity; 812; Rabbit; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; project #745-88; 11/8/88; DPX-E9636-22 technical; 2000 mg/kg of test article (moistened w/dimethyl phthalate) applied to clipped, intact skin; 24 hr

exposure under occlusive wraps; 5M/5F; no deaths; no overt toxic signs; slight weight losses occurred in some animals; necropsies were not done; LD_{50} (M/F) > 2000 mg/kg; Toxicity Category III; **Acceptable**. (Rubin, 3/4/93)

Acute inhalation toxicity, rat **

51932-041; 121141; Acute inhalation toxicity; 813; Rat; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; project #628-89; 1/17/91; DPX-E9636-22 technical; 4.8 and 5.4 mg/L gravimetric concentrations (MMAD=2.3 & 2.4 mm, respectively); 5/sex/dose; 4 hr nose only exposure; no deaths; slight ocular and nasal irritation either immediately after or 1 day following exposure, slight body weight depressions in 10/20 animals for 1 day and, transiently, in all females for the entire 14 day observation period; 2/20 rats developed slight hair loss either on the shoulders or paws by day 14 post dose; terminal necropsies revealed no organ specific toxicity; LC_{50} (M/F) > 5.4 mg/L; Toxicity Category IV; **Acceptable. (Rubin, 3/4/93)

Primary eye irritation, rabbit **

51932-040; 121140; Primary eye irritation; 814; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; project #712-88; 10/24/88; DPX-E9636-22 technical; 0.1 ml (73 mg) instilled into the conjunctival sac of the left eyes of 4 males and 2 females; grade 1 corneal opacity and iritis in 6/6 animals at 1 hr post dose, clearing completely by 24 hr; conjunctival irritation: grade 2 (due to chemosis) in 6/6 at 1 hr, grade 2 (due to redness) in 1/6 at 24 hr, all positive reactions clearing by 48 hr; slight blood-tinged discharge in 1 rabbit at 1 hr; all eyes appeared normal by 72 hr; Toxicity Category III; **Acceptable. (Rubin, 3/5/93)
51932-086 133982 This is a supplement to Record No. 121140, containing updated QA and GLP assurance, a summary sheet of ocular responses, and individual data. There is no change from the above category assignment. Aldous, Nov. 3, 2015.

Primary dermal irritation **

51932-042; 121142; Primary dermal irritation; 815; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; project #733-88; 11/3/88; DPX-E9636-22 technical; 0.5 ml, moistened with dimethyl phthalate, was applied to gauze and placed on clipped, intact test sites; 4 males, 2 females; 4 hr exposure; neither erythema nor edema were observed at any time through 72 hr post dose; Toxicity Category IV; **Acceptable. (Rubin, 3/5/93)

Dermal sensitization **

**51932-0087 133983) Armondi, S., "Maximization Sensitization Study (Magnusson-Kligman) with DPX-E9636-22 in Guinea Pigs (Revision No. 1, Includes Protocol)," 7/26/90, Haskell Laboratory (du Pont), Du Pont HLO 444-90. This study was reviewed by R. Bireley on Sept. 5, 1995. Study was acceptable, and negative for sensitization.

**51932-0043 121143 Brock, W. J., "Closed-patch repeated insult dermal sensitization study (Buehler method) with DPX-E9636-22 in guinea pigs," Haskell Laboratory (du Pont, Newark, DE), 6/20/1989, du Pont HLR 32-89. Duncan Hartley guinea pigs were assigned DPX-E9636-22 (rimsulfuron) treatment (5/sex), negative control (2M,3F), or positive control (3M,2F). Rimsulfuron [70% suspension in EtOH:H_2O (80%:20%)] animals received 3 induction treatments at weekly intervals, followed 2 weeks later by challenge. Duration of any given treatment was 6 hours, with application area secured under a patch. All treatments were 0.4 ml volume. Positive control [0.1% suspension of 1-chloro-2,4-dinitrobenzene (DCNB) in

EtOH:H_2O (80%:20%)] was administered on the same schedule. Negative controls were treated in challenge phase only, with 0.4 ml rimsulfuron suspension and 0.4 ml DCNB as above. One of the 10 rimsulfuron animals had a slight erythema at the final induction phase, and again at challenge (at 24 hr and at 48 hr examination). All negative control results gave negative skin responses. All positive control animals had scores of at least 2 at the second and third induction phases. At challenge, average positive control scores at 24 and 48 hours were 3.0 and 2.4, respectively. Test article is negative for dermal sensitization. Study is acceptable. Aldous, Nov. 5, 2015.

SUBCHRONIC STUDIES

Subchronic oral toxicity, rodent: **

** 51932-088; 133984; "Subchronic Oral Toxicity: 90-Day Study with IN E9636-21, Feeding Study and One-Generation Reproduction Study in Rats", M.S. Bogdanffy; 821; Rat; E.I. du Pont de Nemours and Company, Inc., Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Report No. 43-89; 9/14/89; Rimsulfuron (IN E9636-21 Technical, purity: ≥ 97.5%); 20 animals/sex/group; Doses: 0, 50, 1,500, 7,500, or 20,000 ppm in the diet (males: 0, 3.35, 102, 495, 1,311 mg/kg/day; females: 0, 4.11, 120, 615, 1,622 mg/kg/day, respectively); **Subchronic Feeding Study:** No mortality; Clinical Signs: reduced body weight gain (M:1500, 7500, 20000 ppm); Hematology: reduced RBC count, hemoglobin, hematocrit, and WBC, lymphocyte counts (F:20000 ppm, 90 days); Clinical Chemistry: increased calcium (M:7500, 20000 ppm, 90 day), increased cholesterol, total protein, globulin (M:20000 ppm, 90 day), increased sodium (M:7500, 20000 ppm, 45, 90 days), reduced calcium (F:7500, 20000 ppm, 90 day), reduced phosphorus (F:1500, 7500, 20000 ppm, 90 day), reduced bilirubin (20000 ppm, 45, 90 days); Urinalysis: reduced pH (M:1500, 7500, 20000 ppm, 90 day), increased volume (F:20000 ppm, 45, 90 days), reduced osmolarity (F:20000 ppm, 90 day); Necropsy: increased absolute and relative liver weight (M/F:7500, 20000 ppm); Histopathology: hepatocellular centrilobular hypertrophy (M/F: 7500, 20000 ppm); **No adverse effects**; **Target organ**: liver; **NOEL:** 50 ppm (based upon reduced body weight gain and other apparent treatment-related effects in 1500 ppm treatment group); **NOAEL:** > 20000 ppm; Study acceptable.

One-Generation Reproduction Sub-study: Maternal-no mortality; no treatment-related signs of toxicity reported; no apparent treatment-related effect upon mating, fertility or gestation indices; Offspring-no treatment-related effects upon pup viability or body weight; Study supplemental. (Moore, 4/14/95)

51932-022; 116384; 90-day chronic feeding; 821; Mouse; E.I. du Pont de Nemours & Co, Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 10/19/89; report #3-89 (author: M.S. Bogdanffy); Rimsulfuron (IN E9636-21; 94-99% purity) was incorporated into diet at 0, 50, 375, 1500, & 7500 ppm; no treatment-related clinical signs, ophthalmic effects, or histologic changes; body weight gain in males was reduced by 12.5% and 17.5% at 1500 and 7500 ppm (not statistically significant); red blood cell counts, hemoglobin concentration, and hematocrit were significantly increased in males at 1500 ppm (45 and 90 days) and 7500 ppm (90 days only) (female mice were unaffected); relative spleen weights were also increased in males at 7500 ppm; reported NOEL (M/F) = 7500 ppm, (M = 1220 mg/kg/day; F = 1575 mg/kg/day, no effect at HDT); **Unacceptable (but possibly upgradeable upon submission of clinical chemistry data).** (Rubin, 1/27/93)

Subchronic Oral toxicity, non-rodent: ** †

****51932-023; 116385;** 90-day chronic feeding; 821; Dog; E.I. du Pont de Nemours & Co, Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 10/30/89; report #604-89 (author: D.A. Keller): rimsulfuron (IN E9636-22; 99-101% purity) was incorporated into diet at 0, 250, 5000, or 20,000 ppm; no treatment-related clinical signs, ophthalmic effects, or histologic changes were detected; a slight inverse correlation related dose to body weight, body weight gain, and mean daily food consumption (occasional statistical significance at the high dose); a change in liver function was apparent in the increased serum alkaline phosphatase (high dose), increased cholesterol (mid and high doses), decreased albumin concentration (high dose), and increased globulin concentration (high dose); evidence for an osmotic diuretic effect included an increased urine volume and decreased urine osmolality in both sexes; liver and kidney weights increased (mid and high doses) and heart weights declined somewhat (high dose); **possible adverse effect:** testicular degeneration at the mid and high dose; NOEL, M=9.63 mg/kg/day, F=10.6 mg/kg/day, M/F=250 ppm (based on adaptive changes of the liver and testicular degeneration); **Acceptable.** (Rubin, 1/26/93)

Dermal toxicity, 21/28-day or 90-day:

CHRONIC STUDIES

Combined (Chronic and Oncogenicity), rat **

51932-025; 116387; 2-yr combined chronic toxicity/oncogenicity; 835; Rat; E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 1/31/90; report #559-90 (author: D.A. Keller); rimsulfuron (IN E9636-22, 98.8% purity) was incorporated into the diet at 0, 25, 300, 3000, & 10,000 ppm; 62 rats/sex/dose; interim sacrifice at 1 yr: 10 rats/sex/dose; mortalities: after 1 yr the high dose males showed a statistically significant increase in deaths (7 vs 0 in controls @ 371 days); the lower survival rate persisted until end of 2nd yr when high control death rate eradicated the difference; no treatment-related mortality in females; males & females showed statistically significant depressions of body wt or wt gain at or during the 1st yr which persisted to some degree during the 2nd yr, but w/o statistical significance; no sustained effect on food consumption or food efficiency; no toxic signs; no ophthalmologic effects; no significant increase in tumors, gross lesions, masses, or nodules; slight effects on serum parameters at 1 and 2 yr at the high dose probably due to adaptive liver changes; relative liver & kidney wts significantly increased at 1 yr (liver only at 2 yr); NOEL (M/F) = 3000 ppm (M=121 mg/kg/day, F=163 mg/kg/day, based on liver weight and enzyme changes and male body weight changes); **no adverse effects; Acceptable. (Rubin, 2/2/93)

51932-0092 133989 Amendment to above combined study.

Chronic, dog ** †

****51932-050; 121158;** Chronic toxicity; 831; Dog (Beagle); Bio/dynamics Inc., East Millstone, NJ; "A Chronic (1 Year) Oral Toxicity Study in the Dog with IN E9636-22 Via the Diet"; author, J.E. Atkinson; project #89-4952; 1/4/91; rimsulfuron (IN E9636-22; 98.8% purity) was administered in the diet at 0, 50, 2500, & 10,000 ppm for 1 yr; 5/sex/dose; no deaths; no effect on food consumption; high dose females gained less weight than controls (1.9 vs. 4.1 kg), though

this may be due to 2 abnormally large females in the control group; corneal opacity due to lipidosis occurred in 1/5 males & 2/5 females at the high dose by 32 wks, though it had partially resolved by the time of the terminal exam; serum cholesterol and alkaline phosphatase were elevated in mid and high dose animals indicating changes in liver activity; urine volume were occasionally increased at the mid & high doses, as were liver & kidney weights & tracheal mucosal hyperplasia; **possible adverse effects:** testicular degeneration and epididymal changes**;** NOEL, M/F, = 1.6 mg/kg/day (50 ppm, based on cornea opacity, liver enzyme changes and testicular degeneration); **Acceptable.** (Rubin, 3/12/93)

Record Nos. 121156 and 121157 were supplemental to Record No. 121158, above.

Oncogenicity, mouse ** †

****51934-046/047; 121154/121155;** Oncogenicity; 832; Mouse; E.I. du Pont de Nemours & Co, Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; "Oncogenicity Study with IN E9636-22; 18-Month Feeding Study in Mice"; author, D.A. Keller; project #732-90; 1/18/91; rimsulfuron (IN E9636-22; 98.8%) was administered in the diet at 0, 25, 250, 2500, & 7500 ppm for 18 months; 80/sex/dose; no compound related deaths; high dose male & female body wts and female wt gains were significantly reduced, causing significant increases in relative liver, testes, heart, & kidney wts; no changes in palpable masses, clinical observations, or hematological parameters; **possible adverse effects:** high dose females had increased eye anomalies (mostly cataracts) by the end of the expt. (18/61 vs. 5/58 in controls); high dose males had increased benign tumors (28/80 vs. 17/80 in controls, $p \leq 0.05$), decreased malignant tumors and increased incidence & severity of testicular artery and tunica degenerations (73/80 vs. 20/80 in controls, $p \leq 0.05$); NOEL (M/F) = 2500 ppm (M = 351 mg/kg/day, F = 488 mg/kg/day, based on eye anomalies and testicular artery and tunica degeneration); **Acceptable.** (Rubin, 3/22/93)

51932-0052 125900 Supplement to Record No. 121154, above.

GENOTOXICITY

Bacterial reverse mutation assay **

** 51932-028; 116390; Mutagenicity *Salmonella typhimurium* reversion to histidine independence); 842; *Salmonella typhimurium*; E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 4/3/89; report #132-89; rimsulfuron (DPX-E9636-22, 98.8% purity); doses: 0, 50, 100, 250, 500, 750 mg/plate (high dose based on cytotoxicity); 48 hr exposure; duplicate cultures, 2 independent trials for each condition; tester strains TA1535, TA97, TA98, & TA100 exposed to sodium azide, acridine, 2-nitrofluorene, and sodium azide, respectively, as positive controls w/o S9 microsomal activation, and 2-aminoanthracene w/S9 activation; cytotoxicity seen in preliminary mutagenicity assay w/o S9 in TA1535 @ 500 mg/plate & in TA97, TA98, & TA100 @ 1000 mg/plate, w/S9 in TA1535 @ 500 mg/plate & in TA97, TA98, & TA100 @ 2500 mg/plate; no increase in back-mutation to histidine independence seen at any test article concentration regardless of the absence or presence of S9 microsomal activation; **Acceptable**. (Rubin, 2/4/93)

**51932-0091 133988 Reynolds, V. L., "Mutagenicity testing of DPX-E9636-22 in the Salmonella typhimurium plate incorporation assay," (du Pont) Haskell Laboratory, Newark, DE, 2/21/92. Study: HLR 104-92. *Salmonella typhimurium* strains TA 1535, TA 100, TA 97, and TA 98 were used on DPX-E9636-22 (Rimsulfuron, 99.0% purity). There were two separate

plate incorporation experiments, each with triplicate plates at 100, 250, 500, 750, 1000, (usually) 2500, and 5000 µg/plate. Where high dose range toxicity was limiting, additional lower dose levels were used. In more recent years, guidelines have called for use of a fifth strain. The strains used were a complete set for then-contemporary studies. No treatment elicited increased revertants to the limits of toxicity. All positive controls were functional. Study is acceptable. Aldous, 11/5/15.

Mutagenicity: *In vitro* mammalian cell assay **

** 51932-026; 116388; Mutagenicity; 842; CHO-K1 cells (clone BH4); E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 9/20/89; report #423-89; Rimsulfuron (DPX-E9636-22, 98.8% purity); doses: 0, .01, .10, .25, .75, & 1.3 mg/ml (the highest soluble dose); 2 non-activated (18-19 hr exposure) and 2 activated (5 hr exposure) trials; after test article exposure cells were sub-cultured 2x over a 1 wk period before replating under selective conditions (10^{-5} M 6-thioguanine); positive controls: 0.5 mM methanesulfonic acid (non-activated) and .015 mM DMBA (activated); neither cytotoxicity nor mutagenicity was observed in any trials; cytotoxicity tests at 1.3 mg/ml test article (the high dose) w/o S9 microsomes yielded survival rates between 91.7% and 96.3% of controls, paralleling mutation frequencies (mutants/106 surviving cells) between 0 and 6.9 (negative controls ranged from 0 to 6.4, positive controls from 159.3 to 218.2); in the presence of the S9 microsomes cytotoxicity at 1.3 mg/ml ranged from 68.4% to 113.4% of controls and mutation frequency ranged from 0 to 15.6 (negative controls ranged from 0 to 11.1, positive controls with DMBA from 124.0 to 190.3); **Acceptable**. (Rubin, 2/3/93)

Mutagenicity: *In vivo* cytogenetics **

** 51932-029; 116391; Structural chromosome aberration; 843; human lymphocytes; E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 2/4/89; report #346-89; rimsulfuron (DPX-E9636-22, 98.8% purity); doses: 0, 0.1, 0.6, 1.0, & 1.3 mg/ml (high dose based on peak solubility); 3 hr exposure; no change in # aberrations/cell, % aberrant cells, % of cells with greater than 1 aberration, or mitotic index was observed at any rimsulfuron concentration in the absence or presence of S9-mediated metabolic activation; positive controls: mitomycin C (-S9) increases the # of aberrations/cell over negative controls by 16.5-42-fold, the % abnormal cells by 10-32-fold, and the % of cells with greater than 1 aberration from 0 to 8-16%; cyclophosphamide (+S9) generated increases in # of aberrations/cell of 8.7-26-fold, % of abnormal cells of 8-22-fold, and the % of cells with greater than 1 aberration from 0 to 2-8%; no effect on any ~7type~1 of aberration was detected; both positive controls showed increases in various types of chromosomal aberrations (particularly chromatid gaps); rimsulfuron does not elicit clastogenic changes under the conditions tested; **Acceptable**. (Rubin, 2/5/93)

** 51932-030; 116393; Structural chromosome aberration (micronucleus assay); 843; mouse (bone marrow polychromatic erythrocytes); E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 9/13/89; report #480-89; rimsulfuron (DPX-E9636-22, 98.8% purity); doses: 0, 500, 3000, & 5000 mg/kg body weight; administered by gavage; no increase in multinucleated PCE's nor any change in the mean PCE/NCE (normochromatic erythrocyte) ratio; the positive control, cyclophosphamide, induced a 9.25-fold rise compared to negative controls in mean % micronucleated PCE's among males

and a 5.8-fold rise among females (no change in PCE/NCE ratio); rimsulfuron does not induce micronuclei under the present conditions; **Acceptable**. (Rubin, 2/5/93)

DNA Damage (no longer a required tier 1 study) **

** 51932-027; 116389; Other genotoxic effects; (unscheduled DNA synthesis); 844; primary rat hepatocytes; E.I. du Pont de Nemours & Co., Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; 9/20/89; report #418-89; rimsulfuron (DPX-E9636-22, 98.8% purity); doses: 0, .0008, .004, .008, .04, .08, .4, .8, & 1.1 mg/ml (high dose close to solubility limit); 18 hr exposure; duplicate cultures, 2 independent trials; positive controls: 2-acetyl aminofluorene, .02 & .2 mg/ml; cytotoxicity, determined by assay of lactate dehydrogenase in medium after test article exposure, was minimal; no unscheduled DNA synthesis was detected at any concentration tested; mean net nuclear grains/cell (mNNG), calculated by subtracting the mean cytoplasmic grains/cell from the mean nuclear grains/cell, was always negative, even at the high dose (in Trial 1 the mNNG/cell at 1.1 mg/ml = -9.1, in Trial 2 = -3.5); positive controls ranged in the 2 trials from a mNNG/cell count as low as 17.2 at 0.02 mg/ml to as high as 48.3 at 0.2 mg/ml; **Acceptable**. (Rubin, 2/3/93)

REPRODUCTIVE TOXICITY, RAT **

51932-045; 121152; Multigenerational reproductive toxicity; 834; Rat; E.I. du Pont de Nemours & Co, Inc., Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE; "Reproductive and Fertility Effects with IN E9636-22 Multigeneration Reproduction Study in Rats"; author, L.S. Mullin; project #203-90; 9/12/90; Rimsulfuron (IN E9636-22) was administered in the diet at 0, 50, 3000, & 15,000 ppm to P_1 rats (30/sex/group) for 74 days before breeding within the dose groups; compound administration to P_1 animals continued during breeding, gestation, & lactation, followed at weaning by 105 days of administration to F_1 animals before breeding within the dose groups (30/sex/group) to produce the F_2 generation; deaths: 1 P_1 female, 1 F_1 male, & 1 F_1 female at 15,000 ppm, and 1 F_1 female at 3000 ppm; deaths appeared to be of unrelated causes; significantly lower body wt. in high dose F_1 males (by 7 days post weaning) and F_2 pups (mid dose F_1 males & high dose F_1 & P_1 females had a similar tendency); lowered food intake in premating mid & high dose F_1 males (not P_1 males); no effect on clinical signs or reproductive indices in P1 or F_1 adults, or F_2 pups (except for weight losses noted above); pathology exams were negative; Maternal NOEL=15,000 ppm (1021 mg/kg/day, no effect at HDT); Reproductive NOEL-3000 ppm (204 mg/kg/day, reduced pup weight); **No adverse effect; Acceptable. (Rubin, 3/18/93)

DEVELOPMENTAL TOXICITY

Rat **

** 51932-024; 116386; Teratology; 833; Rat; Haskell Laboratory for Toxicology and Industrial Medicine, Du Pont, Inc., Newark, DE; project #170-89 (author: L. Alvarez); 7/28/89; Rimsulfuron (IN E9636-22) was administered by gavage on days 7-16 of gestation; 0, 200, 700, 2000, & 6000 mg/kg; maternal effects, high dose: significantly decreased wt. gain, days 11-13, significantly reduced feed consumption, days 9-15, and altered fecal color; no significant effects on pregnancy rate, corpora lutea, nidations or resorptions/dam, or litter size; fetal weights, ~7in utero~1 survival, and incidence of variations and malformations were unaffected by the

treatment; maternal NOEL = 2000 mg/kg/day, fetal NOEL = 6000 mg/kg/day; **Acceptable**. (Rubin, 1/28/93)

Rabbit **

51932-044; 121150; Teratology; 833; Rabbit; Haskell Laboratory for Toxicology and Industrial Medicine, Du Pont, Inc., Newark, DE; "Teratogenicity Study of IN E9636-22 in Rabbits" (author: L. Alvarez); project #403-89; 9/22/89; rimsulfuron (IN E9636-22; 98.8% purity) was administered by gavage on days 7-19 of gestation to animals impregnated by artificial insemination; 0, 25, 170, 500, & 1500 mg/kg; ~7maternal effects~1; deaths: 0/20, 0/20, 0/20, 1/20, & 15/20; no effects on maternal wt. changes; significantly decreased maternal feed consumption during the dosing pd. at the 500 mg/kg/day dose (129.9 g/dam/day vs. 143.1 g/dam/day in controls, $p \leq .05$; not enough pregnant survivors at the high dose to permit interpretation); clinical observations: weakness, abortion, & cageboard staining; no fetal effects observed (~7i.e.~1 no test article related weight changes, no malformations, no variations); maternal NOEL = 170 mg/kg/day (based on mortality); developmental NOEL > 1500 mg/kg/day (no effect at HDT); **no adverse effect, **Acceptable.** (Rubin, 3/9/93)
51932-0090 133987, 51932-0089 133985 (Supplementary data to Record No. 121150, above).

NEUROTOXICITY

Acute neurotoxicity, rat

90-day neurotoxicity, rat

Developmental neurotoxicity, rat

Delayed neurotoxicity, hen

IMMUNOTOXICITY

ENDOCRINE DISRUPTOR STUDIES

SUPPLEMENTAL STUDIES

51932-0170 286627 Scheres, H. M. E., "Evaluation of the mutagenic activity of IN-E6758 (RCC NOTOX Substance 11592) in the Ames *Salmonella*/microsome test (with independent repeat)," RCC NOTOX B.V., 's-Hertogenbosch, The Netherlands, 11/27/90. Laboratory Study # RCC NOTOX 044234. Investigators performed two independent reverse mutation plate incorporation tests employing strains TA 1535, TA 100, TA 1537, and TA 98 to evaluate IN-E6758 (a rimsulfuron impurity), Batch E52691-89-3B22, at concentration about 100%. Each test used triplicate plates at 100, 333, 1000, 3330, and 5000 µg/plate, with DMSO as negative control vehicle. Positive controls were functional. Strain TA1537 elicited several-fold increases in revertants at 5000 µg/plate in both tests, with and without S9. Further, Strain 1537 consistently displayed at least 2-fold increase in inversions at 3330 µg/plate. There was no response at 1000 µg/plate or below with strain 1537. Other strains showed no treatment effects. No cytotoxicity was evident. Response is a "possible adverse effect," as high concentrations of this impurity were shown to elicit frameshift mutations in strain TA1537. Aldous, Nov. 5, 2015.

51932-0054 132121 "General pharmacological study of rimsulfuron," Study No. 3L409, Mitsubishi-Kasei Institute of Toxicological Sciences, translation dated 5/23/94. Groups of 3 male CD-1 mice were dosed once by gavage at 100, 300, 1000, or 3000 mg/kg. Mice were observed at 0.5, 1, 2, 4, and 24 hours. The only alteration observed was slightly reduced spontaneous behavior at 3000 mg/kg at 1-2 hours. In another test, 4 anesthetized Japanese White rabbits per group were dosed once *iv* at 0, 0.2, 2, or 20 mg/kg to assess respiration, blood pressure, heart rate, and EKG. Observations were taken for up to 20 minutes. There were no changes in any of these parameters. This is a supplementary study, not of any guideline design, and not indicative of any key toxicological endpoints. There is no DPR worksheet. Aldous, 11/3/15.