MEMORANDUM

SUBJECT: 5H05727; 5F04554; 010182-00324. Touchdown® Herbicide. Application for Amended Registration for Use on Apples, Crabapples, Loquat, Pear, Quince and Wheat

PC Code 128501
Tox. Chem. No. 893C

Project Nos. D217444, D217454, D217460
Submission Nos. S490509, S490506, S490457

TO: Terri Stowe, PM Team # 25
Registration Division (7505C)

FROM: Pamela M. Hurley, Toxicologist, Section I, Toxicology Branch I
Health Effects Division (7509C)

THRU: Roger L. Gardner, Section Head
Section I, Toxicology Branch I
Health Effects Division (7509C)

Background and Request:

Zeneca Ag Products has submitted an application for amended registration for use of Touchdown® Herbicide on pome fruit and wheat. Section F of the application (the proposed tolerance) was not submitted to the Toxicology Branch, but it is assumed that the tolerances will be for glyphosate-trimesium in or on the selected commodities. The submitted label for pome fruit and wheat is for Touchdown® Herbicide, containing 57.6% active ingredient. It contains 6 pounds active ingredient per gallon. It is to be applied as a broadcast and/or a spot spray. The herbicide may also be applied using a wiper or "wick" applicator. TB-I has been asked to determine whether or not the toxicology data base supports these requested tolerances.
**Toxicology Branch Response:**

TB-I has determined that the toxicology data base for this chemical is complete. TB-I has no objection to granting the application for amended registration for use of Touchdown® Herbicide on pome fruit and wheat, provided that the tolerances are for glyphosate-trimesium in or on the selected commodities.

The following summarizes the toxicity testing requirements for the requested uses and tolerances. A Toxicity Profile is attached for the technical material.

**Data Requirements (CFR 158.135):**

**Technical:** Glyphosate Trimesium  
**Use Pattern:** Herbicide; broadcast and/or spot spray; wiper or "wick" applicator.  
**Action Type:** Amended Registration  
**Last Updated:** 08/22/94

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<th>Requirement</th>
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<th>Satisfied</th>
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<td>81-1 Acute Oral Toxicity</td>
<td>Yes</td>
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<td>81-2 Acute Dermal Toxicity</td>
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<td>81-4 Primary Eye Irritation</td>
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<td>81-5 Primary Dermal Irritation</td>
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<td>81-6 Dermal Sensitization</td>
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<td>81-7 Acute Delayed Neurotoxicity</td>
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<td>82-1(a) Subchronic Oral (rodent)</td>
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<td>83-1(a) Chronic Toxicity (rodent)</td>
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<td>83-1(b) Chronic Toxicity (nonrodent)</td>
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<td>83-2 Oncogenicity (mouse)</td>
<td>Yes</td>
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<td>83-4 Multigeneration Reproduction</td>
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<td>84-2(b) Mutagenicity - Structural Chromosomal Aberrations</td>
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SULFOSATE (Caswell No. 893C; PD No. 128501)

SULFOSATE TECHNICAL (52% a.i.)
Updated 08/22/94

81-1 Acute Oral Toxicity in Rats.
LD₅₀ = 748 mg/kg (males)
LD₅₀ = 755 mg/kg (females)
MRID 249802
Doses used: 500, 550, 600, 700, 800,
STAUFFER CHEMICALS and 900 mg/kg by gavage
# T11185
Signs: mild to severe depression,
November, 1982.
prostration, tremors,
Acceptable
and slow/shallow respiration.
Product tested: SC-0224 62% a.i.

TOXICITY CATEGORY: 3

81-2 Acute Dermal Toxicity in Rabbits
LD₅₀ > 2000 mg/kg (Both sexes; intact or abraded skin).
MRID 249802, 260508
Doses used: 800 -2200 mg/kg.
STAUFFER CHEMICALS
Signs: Rabbits with abraded skin
# T-11185 showed mild to severe depression
November, 1982.
at all doses levels and mild to
Acceptable moderate erythema. Rabbits with skin
intact showed mild depression and
mild erythema.
Product tested: SC-0224 62% a.i.

TOXICITY CATEGORY: 3

81-3 Acute inhalation toxicity in rats
LC₅₀ > 6.9 mg/L (both sexes, 4-hr, whole body exposure)
MRID 249802
Actual chamber concentration:
STAUFFER Chem No. 6.9 mg/L
T-11084
MMAD = 3.5 um at 64 min.
November, 1982
2.8 um at 184 min.
Acceptable
SIGNs: wet fur, salivation,
Product tested: Sulfosate (62% a.i.)
chromorhinorrhea

TOXICITY CATEGORY 3
Acute inhalation toxicity in rats
LC₅₀ > 5.18 mg/L (4-hr, nose only exposure)
Actual chamber concentration: 2.65-6.3 mg/L
MMAD: 4.56 ± 2.06 µm
[20% < 2.5 µm (inhalable) & 3.9% < 1 µm (respirable)]
No mortality observed.
SIGNS: (CNS & Autonomic) salivation, splayed gait, head & paw flicking, tail erection, shaking, subdued behavior, slow/deep breathing, decrease response to sound. Effects subsided on day 2.
A limit test was not reached since only 3.9% of the aerolised sulfosate particles were of respirable size (EPA requires 25%).
Product tested: Sulfosate 57.6% a.i. and
This study may be upgraded to acceptable when evidences are provided to show that optimum technology was used in generating the sulfosate containing aerosol.

TOXICITY CATEGORY:

Primary Eye
Irritation in Rabbits
LC₅₀ > 5.18 mg/L (4-hr, nose only exposure)
Actual chamber concentration: 2.65-6.3 mg/L
MMAD: 4.56 ± 2.06 µm
[20% < 2.5 µm (inhalable) & 3.9% < 1 µm (respirable)]
No mortality observed.
SIGNS: (CNS & Autonomic) salivation, splayed gait, head & paw flicking, tail erection, shaking, subdued behavior, slow/deep breathing, decrease response to sound. Effects subsided on day 2.
A limit test was not reached since only 3.9% of the aerolised sulfosate particles were of respirable size (EPA requires 25%).
Product tested: Sulfosate 57.6% a.i. and
This study may be upgraded to acceptable when evidences are provided to show that optimum technology was used in generating the sulfosate containing aerosol.

TOXICITY CATEGORY:
Primary Dermal Irritation in Rabbits
MRID 249802
STAUFFER CHEMICALS
# T-11185
November, 1982.
Acceptable

24-hr exposure. Effects at 24 hr: intact and abraded skin showed mild erythema. Mild edema observed in 3/6 rabbits with skin abraded and 1/6 rabbits with skin intact. All dermal effects reversed within 72 hrs. Primary Irritation Score: 0.67. Dose used: 0.5 ml SC-0224 62% a.i.

TOXICITY CATEGORY: 4

Dermal Sensitization in Guinea Pigs
MRID 258398
Richmond Tox. Labs.
# T-11269
October 12, 1984.
Acceptable

SC-0224 Technical (56.3% a.i) is a mild skin sensitizier (Open Epicutaneous Test)
81-7  Acute Delayed Neurotoxicity Study in Hens
MRID 431512-01
ICI Toxicology Labs
CA/# T-12324;
4/18/89
Core Minimum

NOEL: for systemic toxicity: 500 mg/kg
LEL: for systemic toxicity: 5000 mg/kg

Effects: Administered by gavage at 0, 500 or 5000 mg/kg in 5 ml/kg water. TOCP (500 mg/kg) was positive control. 6 hens/group in control groups, 8 hens/group in treated groups. Each animal dosed twice during study; day 1 & day 22. Each animal evaluated up to day 41 (or 42). 500 mg/kg: diarrhea for 2-3 days, starting a few days after each dosing. 5000 mg/kg: diarrhea, changes in comb appearance, early ↓ food consumption & ↓ in egg production observed. No indications of neurotoxicity were observed. The positive control indicated the appropriate clinical signs of toxicity, increased ataxia and microscopic observations for an organophosphate. Study is core minimum because it was conducted prior to the publication of the new neurotoxicity guidelines which were published in 1991.

81-8  Acute Mammalian Neurotoxicity Study in Rats
MRID 431323-01
Zeneca Central Tox. Labs
#’s AR5425;
CTL/P/3813
2/15/93
Core Guideline

NOEL: 100 mg/kg
LEL: 300 mg/kg

Effects: Alpk:APfSD rats. Doses: 0, 30, 100 or 300 mg/kg. Positive control data provided. 300 mg/kg: death, ptosis, ↓ activity, ↓ splay reflex, upward curvature of spine, chromodacryorrhea, shaking, sides pinched in, signs of urinary incontinence, irregular breathing, hunched posture, abnormal or staggering gait, staining around nose, ↓ bodyweight (♂), ↓ food consumption (♂), ↑ time to tail flick, ↓ landing foot splay, ↓ forelimb grip strength, ↓ hindlimb grip strength, ↓ motor activity. Effects reversible. No microscopic evidence of neurotoxicity. No indications of neurotoxicity below a lethal dose (300 mg/kg).
82-1(A) Subchronic feeding rat
MRID 412099-02
Stauffer Chem
No. T-10888
4-3-87
Acceptable

NOELs: 800 ppm (MDT, 36 mg/kg/day) in males and 2000 ppm (HDT, 108 mg/kg/day) in females.
LOEL: 2000 ppm (88 mg/kg/day) in males, based on a significant overall decrease in body weight gain (22% below controls).
The HDT only caused sporadic and minimal decreases in body weight in females (secondary to a feed palability - related reduction in feed intake) and no significant overall decrease in B.W. gain.
No significant changes were observed in clinical chemistry, hematology, urinalysis, organ weights, or macroscopic/microscopic histopathology.
Doses tested: 0, 150, 350, 800, and 2000 ppm.
MTD was reached for males only.
Product tested: Sulfosate (19.2% a.i., 75.6% water)

82-1(b) Subchronic feeding dog
MRID 412099-02/03
Stauffer Chem
No. T-11002
4-3-87
Acceptable

NOEL: 10 mg/kg/day (MDT)
LOEL: 50 mg/kg/day (HDT) based on increase incidences and earlier onset of emesis and salivation.
No changes in B.W., food consumption, clinical chemistry, hematology, urinalysis, organ weights, or macroscopic/microscopic histopathology were observed.
Doses tested: 0, 2, 10, and 50 mg/kg/day by gavage.
Dog's Strain: Beagle
Product tested: Sulfosate (19.2% a.i., 75.6% water)

82-2 21-day dermal - rabbit
MRID 408937-02
Hazleton
No. HLA6142-107
3-1-88
Guideline

Systemic NOEL: 1000 mg/kg/day (HDT)
Mild erythema at application sites in all treated groups.
Doses tested: 0, 10, 100, and 1000 mg/kg/day 6 hrs/day; 5 days/week; 3 weeks.
Product tested: Sulfosate (57.3% a.i.).
82-7 Subchronic mammalian neurotoxicity rat MRID 431512-02 Zeneca Central Tox. Labs Study #’s PRO887; CTL/P/3831 2/15/93 Core Guideline

NOEL: .600 ppm (47.6 mg/kg/day) LOEL: 2000 ppm (153.2 mg/kg/day) Effects: Alpk:APfSD rats: 0, 200, 600 or 2000 ppm (0, 15.6, 47.6 or 153.2 mg/kg/day for males; 0, 18.2, 54.4 or 171.0 mg/kg/day for females) in diet for 90 days. 12/sex/dose group. Positive control data were provided. 2000 ppm: ↓ body weights, food consumption & utilization, ↓ mean forelimb grip strength values (?). No microscopic evidence of neurotoxicity. Evidence for neurotoxicity is not clear.

83-1a Feeding/Oncogenic (2-year) in Mice MRID 402140-06 412099-07 Stauffer Chem No. T-11813 4/3/87 Guideline

Systemic NOEL: 1000 ppm (MDT) Systemic LOEL: 8000 ppm based on decreases in B.W. and feed consumption (both sexes), increases incidences of white matter degeneration in lumbar spinal cord (males only), and increase incidences of duodenal epithelial hyperplasia (females only). Not oncogenic at dose levels up to and including 8000 ppm. Highest dose level may have been excessive. Doses used: 0, 100, 1000, and 8000 ppm Mice strain: Charles River Test material: Sulfoosate 56.17% a.i.

83-1a Feeding/Oncogenic (2-year) in Rats MRID 402140-07 412099-05 Stauffer Chem No: T-11082 4/4/87 Guideline

Systemic NOEL: 1000 ppm (HDT) There were decreases in bodyweight (both sexes) and increased incidences of chronic laryngeal and nasopharyngeal inflammation (males). Bodyweight decrease was considered to be secondary to reduction in food consumption. However, study was acceptable because top dose may be approaching at least 1/2 of an adequate dose for carcinogenicity testing (based on results from subchronic, reproduction studies). Not oncogenic at any level tested. Doses used: 0, 100, 500, and 1000 ppm Rats strain: Charles River CrL:CD (SD) BR. Test material: Sulfoosate 56.17% a.i.
| 83-1(b) | Chronic Feeding (1-year) in Dogs | Systemic NOEL: 10 mg/kg/day (MD)  
Systemic LOEL: 50 mg/kg/day (HD)  
based on decreases in LDH.  
Doses used: 0, 2, 10, and 50 mg/kg/day, by gavage.  
Selection of above dose range was based on (i) a 28-Day oral gavage study in which 150 mg/kg/day was lethal within 3 days and 75 mg/kg/day produced emesis, and (ii) a 90-Day study in which 50 mg/kg/day produced increase in emesis and salivation.  
Dog's Strain: Beagle  
Test material: Sulfosate 56.2% a.i. |
| 83-3(a) | Teratogenicity in Rats | Developmental NOEL: 100 mg/kg/day  
Developmental LOEL: 333 mg/kg/day  
Based on significant decreases in fetal bodyweight  
Maternal NOEL: 100 mg/kg/day.  
Maternal LOEL: 333 mg/kg/day based on undetermined deaths of 2 dams at HDT; decreases in bodyweight, bodyweight gain and feed intake; increased salivation, chromorhinorrhea and lethargy (HDT).  
Doses used: 0, 30, 100, and 333 mg/kg/day by gavage to S-D rats.  
Test material: Sulfosate 19.2% a.i. |
| 83-3(b) | Teratogenicity in Rabbits | Developmental NOEL: 40 mg/kg/day  
Developmental LOEL: 100 mg/kg/day  
(reduction in number of live fetuses/doe, 4 abortions & having only 7 litters does not give sufficiently high # of animals to absolutely conclude that no developmental toxicity is occurring.  
Maternal NOEL: 40 mg/kg/day (MDT)  
Maternal LOEL: 100 mg/kg/day (HDT)  
(6 deaths/17 pregnant does, 4 abortions in 11 survivors, decreased body weight, body weight gain, food consumption).  
Doses used: 0, 10, 40, and 100 mg/kg/day by gavage to Dla:(NZW)SPF rabbits.  
Test material: Sulfosate 56.2% a.i. |
Reproduction
(2-gen) in Rats
Accession Nos:
258399 & 258399
Stauffer Chem.
No: T-110-51
4/19/84
Guideline

Reproductive/Developmental NOEL:
150 ppm (LDT)
Reproductive/Developmental LOEL:
800 ppm (MDT) based on decreased litter size in the F₀a and F₁b litters at 2000 ppm and on decreased mean pup weights during lactation in the second litters at 800 ppm and in all litters at 2000 ppm.
Systemic NOEL: 150 ppm (LDT)
Systemic LOEL: 800 ppm (MDT) based on reduced feed intake, body weights & body weight gains, reduced absolute and sometimes relative thymus, heart, liver & kidney weights.
Doses used: 0, 150, 800, and 2000 ppm in Cr1 CD(SD)Br strain.
Test material: sulfosate 19.2% a.i.

Mutagenicity
Reverse mut. (Ames Test)
in Salmon. Typhi.
MRID 249802
Stauffer Chem.
No: T-10487
1/19/82
Acceptable

Mutagenicity
Reverse mut. (Ames Test)
in Salmon. Typhi.
MRID 260966
Stauffer Chem.
No: T-12660
9/25/85
Acceptable

Not mutagenic at concentrations of 0.12, 0.37, 1.11, 3.33, and 10 mg/plate without S9, and of 0.56, 1.11, 1.67, 3.33, 5.0, 10, and 15 mg/plate with S9.
Tester Bacteria: TA1535, TA1537, TA1538, TA98, and TA100 from Dr. Ames.
Pos. controls: Na azide, 9-aminoacridine (9-AA), 2-nitrofluorene (2-NF), and 2-aminoanthracene (2-AA).
Test material: sulfosate 90% a.i (estimated purity).

Mutagenicity
Reverse mut. (Ames Test)
in Salmon. Typhi.
MRID 260966
Stauffer Chem.
No: T-12660
9/25/85
Acceptable

Not mutagenic at concentrations of 2.5, 5, 10, 20, and 40 ul/plate, with or without S9.
Tester Bacteria: TA1535, TA1537, TA98, and TA100.
Pos. controls: Na azide, 9-AA, 2-NF.
Cytotoxic Dose: HDT
Test material: sulfosate 55.6% a.i.
84-2(a)  Gene Mutation  
(SLRL)  
in Drosophila melanogaster  
MRID 249802  
Litton Bionetics  
No: 22169  
6/13/82  

Acceptable

Not mutagenic at doses of 25 and 50 mg/ml in "Sex linked recessive lethal test".  
Pos. control: EMS

84-2(a)  Gene Mutation  
(Forward Mut.)  
Mouse Lymphoma  
MRID 249802  
Stauffer Chem  
T-10848  
2/8/1982  

Acceptable

Not mutagenic without S9.  
Significant reproducible increase in mutation frequency in presence of S9. Test medium pH not mentioned but was probably in the acid range.  
Indicator cells: L5178Y (TK+/-) mouse lymphoma cell line from Dr. Clive, RTP, No.Carolina.  
Concentrations used: 0.38, 0.75, 1.50, 3, 6, 8, 8.5, 9, and 10 mg/ml in presence of S9, and 0.38, 0.75, 1.5, 3, 6, 7, 8, 9, and 10 mg/ml w/o S9.  
Cytotoxic concentrations: >7 mg/ml

84-2(a)  Gene Mutation  
(forward mut.)  
Mouse Lymphoma  
MRID 260966  
Stauffer Chem.  
No. T-12661  
12/19/1985  

Acceptable

Introduction of sulfosate in the test incubation medium reduced its pH to an acid range (5.67 -7.07). Under this experimental condition, sulfosate was positively mutagenic both in the presence of S9, at concentrations of 3-5 ul test material/ml, or without S9, at concentrations of 3.5 to 5ul/ml. When the pH of test incubation medium was readjusted to a physiological level of 7.4 (Addendum of 3/20,1987), concentrations from 5 to 10 ul/ml lost their mutagenic effect  
Indicator cells: L5178Y(TK+/-) mouse lymphoma cell line (Dr. Clive, RTP, No.Carolina).  
Test material:Sulfosate 55.6% a.i.  
Cytotoxic concentrations:  
Unadjusted acidic medium: >5ul/ml pH adjusted medium: >7.75 ul/ml  
Pos. controls: N-Nitrosodimethyl-amine (DMN) with S9 and Ethyl-methanesulfonate (EMS) wo S9.
Mutagenicity

**Cytogenetic** Rat bone marrow
MRID 249802
Stauffer Chem.
No: T-10884
September 1982
Acceptable

Test animals: 6-wk old CD-Crl:CoBScd(SD)BR male rats.
Not mutagenic (did not induce any structural chromosome aberrations in rats' bone marrow cells.
Doses used: 21, 63, and 188 mg/kg (LD_{50} = 565 mg/kg).
Test material: sulfoate 58.5% a.i.
Pos. control: cyclophosphamide

Mutagenicity

(Micronucleus assay)
Mouse bone marrow
MRID 402140-04
412099-08
Stauffer Chem.
No: EHC-T-12689
4/23/87
Acceptable

Test animals: Charles River D-1 str.
Not mutagenic (did not induce any increase in the number of PCE containing micronuclei).
Doses used: 700, 900, and 1100 mg/kg in males and 400, 600, and 800 mg/kg in females, based on results of a range finding study in which doses >1400 mg/kg killed 3/3 males within 48 hrs and doses >1000 mg/kg killed 2/3 females.

Mutagenicity

(Cytogenetic) in CHO cells
MRID 249802
Stauffer Chem.
No: T-10875
7/6/1982
Acceptable

Positive mutagenicity (induces structural chromosomal aberration in CHO cells both in the absence of S9, at the concentration of 4 mg/ml, and in its presence, at concentrations of 10 and 12 mg/ml.
Sister chromatid exchange (SCE) was not determined.
Concentrations used: 2, 4, and 6 mg/ml w/o S9 and 2; 4, 6, 8, 10, and 12 mg/ml with S9.
Test material: Sulfoate 58.5% a.i.

Mutagenicity

(Cytogenetic) in CHO cells
MRID 249802
Stauffer Chem.
No: T-11019
7/22/82
Acceptable

Positive mutagenicity (Induces structural chromosomal aberration in CHO cells both in the absence of S9, at concentrations of 6-8 ul/ml, and in its presence, at 1-8 ul/ml. No increase in SCE was observed.
Concentrations used: 2, 4, 6, 8, 10, and 12 ul/ml.
Test material: Sulfoate 72% a.i.
84-2(b) Mutagenicity (cytogenetic) in CHO cells
MRID 260966
Stauffer Chem.
No: EHC T-12663
12/18/1985
Acceptable

pH of treatment medium was readjusted to 7.4-7.6 prior to testing.
Not mutagenic (did not induce any structural chromosome aberrations in CHO cells or any increase in SCE) at concentrations of 4-10 ul/ml, with or w/o S9.

Cytotoxic concentrations: None
Pos. controls: Mitomycin C and Cyclophosphamide.
Test material: sulfosate 55.6% a.i.

84-2(b) Mutagenicity (cytogenetic) Mouse Lymphoma
MRID 260966
Stauffer Chem.
No: EHC T-12662
12/19/82
Acceptable

Indicator cells: L 5178Y (TK+/−)
mouse lymphoma cell line from Dr. Clive, RTP, No.Carolina).
Sulphosate concentrations of 5 ul/ml (w/o S9) and >3 ul/ml (w S9) induced chromosomal aberrations in the mouse lymphoma cells and increased the number of SCEs when the pH of the test medium was not readjusted (5.62-7.07). When the pH was readjusted to 7.4 concentrations from 4-10 ul/ml were not mutagenic.

Cytotoxic concentrations: >5 ul/ml at acidic pH, and < 10 ul/ml at physiological pH.
Test material: 55.6% a.i.

84-4 Mutagenicity BALB/3T cells (morphological transformation)
MRID 249802
Stauffer Chem.
No: T-10849
1/4/82
Acceptable

Indicator cells: 1-1 subclone of clone A-31 of BALB/3T3 mouse cells from Dr. Kanunaga (NCI).
Not mutagenic (did not induce an increase in the number of transformed foci)
Concentrations used: 0.313, 0.625, 1.25, 2.5, and 5 mg/ml.

Cytotoxic concentrations: >3 mg/ml
Test material: sulfosate 90% estimated purity.
Test material: (Methyl $^{14}$C) trimethylsulfonium Carboxymethylaminomethylphosphonate) 96.5% purity, 20 mci/mmol.
Identification of the (Methyl $^{14}$C) trimethylsulfonium ion ($^{14}$C-TMS) in urine and fecal extracts done by TLC, GC/MS, autoradiography, and K iodoplatinate spray.
After oral administration of 35 mg/kg (LDT) or 350 mg/kg (HDT) test material to S-D rats of both sexes, the $^{14}$C-TMS ion is rapidly and almost completely absorbed from the GI tract and rapidly excreted unmetabolized mostly via the kidney. Urine recovery of $^{14}$C (expressed as % of administered dose were: 80.8-95% at 24 hr and 91.4-98.5 at 120 hr. Most (95.3-97%) of the total radioactivity was unmetabolized $^{14}$C-TMS ion.
Fecal recovery of $^{14}$C (expressed as % of administered dose were: 0.72-4.03% at 24 hr and 0.95-7.19% at 120 hr. All the radioactivity was unmetabolized $^{14}$C-TMS ion.
$^{14}$CO$_2$ in expired air was negligible.
Tissues residues were negligible: 0-0.148 (LD) and 0-10.6 ppm (HD) sulfosfate equivalents.
The lack of metabolism may be explained by the hydrophilic nature of TMS ion.
Acute toxic effects at the HDT: lethargy, ataxia, slow/labored breathing, salivation, occasional tremors. Signs lessened after 24 hrs.
Metabolism in Rats
MRID 412359-03
ICI Americas Inc.
No: T-12906
12/20/88

Acceptable

Test material: Trimethylsulfonium Carboxymethylaminomethylphosphonate $^{14}$C-radiolabeled on the anionic moiety (Carboxymethylaminomethylphosphonate), 93.2% radiopurity, 9.8 mCi/mmols.

Identification of anion by TLC, autoradiography, and GC/MS.

Males and females S-D rats iv-treated with 25 mg/kg (LDT) test material excreted 90% of the administered dose in urine. After oral administration of the LDT or the HDT (250 mg/kg), the test material was rapidly excreted in urine and feces (70-82% of the total radioactivity administered was excreted within 24 hrs, and 85-94% within 120 hrs).

Absorption was incomplete: only 47-57% of total radioactivity was recovered in urine. Fecal excretion was 36-42% of the administered dose. Most of the recovered radioactivity was unmetabolized carboxymethylaminomethylphosphonate (80-90% of urine and 77-96% of feces total radioactivity). One fecal metabolite was aminomethylphoshonic acid (8.5% of total fecal radioactivity in female rats dosed repeatedly (14 single daily LD of unlabeled test material followed by a single LD of labeled test material).

$^{14}$CO$_2$ in expired air was negligible.

Combined tissue residues were only $\geq0.32%$ of administered dose.

Carcasses contained 2.25% of the administered dose, most of it located in bones.

Acute toxic signs observed with the HD: lethargy, moderate/severe depression, tremors, dehydration, and reduced feed consumption. Signs lasted 72 hours.
Data Gaps: None

Actions Being Taken to Obtain Additional Information or Clarification: N/A

Reference Dose (RfD):

The recommended RfD (to the RfD Workgroup) is 0.1 mg/kg/day. This value was calculated by using the chronic dog feeding study NOEL of 10 mg/kg/day and a safety factor of 100. This RfD has been verified or approved by the Health Effects Division RfD Committee.

Less-than Lifetime Endpoints:

A risk assessment for acute dietary exposure is not required because no appropriate toxicological endpoints were found. The short term (1 to 7 Days) and the intermediate term occupational or residential (1 Week to Several Months) risk assessments are not required because when compared with the oral studies, the 21-day dermal studies indicate that there is not much dermal absorption.

Pending Regulatory Actions: None

Toxicologic Issues Pertinent to This Request:

This chemical has been classified as a Group E Carcinogen: no evidence of carcinogenicity in rat and mouse studies.

Technical sulfosate is usually supplied as an aqueous solution containing about 52% active ingredient. The very viscous nature of sulfosate precludes the practical manufacture of a technical grade with a standard a.i. content (sulfosate forms an intractable glass-like product if its water content is ≤ 30%). The various "technical grade sulfosates" in the "Toxicological Profile" above are either an aqueous sulfosate concentrate containing 62% a.i. or aqueous dilutions of this concentrate to a.i. concentrations of 19.2, 52 or 56.17%.

In some of the in vitro mutagenicity tests conducted in 1982, sulfosate induced a false positive mutagenic effect. These studies were submitted with accession number 249802 (study numbers T-10848 (forward mutation/mouse lymphoma cells), T-10875 (structural chromosomal aberrations/CHO cells) and T-11019 (structural chromosomal aberrations/CHO cells)). A common feature of these tests was that the pHs of the test incubation media were acidic (pH 5.67-7.07) due to the addition of sulfosate. These positive results were no longer observed [accession number 260966 (study numbers T-12661 (forward mutation/mouse lymphoma cells), T-12662 (structural chromosomal aberrations/CHO cells) and T-12663 (structural chromosomal...
aberrations/mouse lymphoma cells)] when the pH was readjusted to a more physiological level (7.4) before the mutagenicity tests were conducted.