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DATA EVALUATION RECORD  
(Addendum of June 3, 1993)

Study Type: Developmental Toxicity  
Guideline §83-3  
Species: Rabbit

EPA Identification No.s: EPA Accession No. 260966  
EPA Pesticide Chemical Code: 128501  
Toxicology Chemical Code: 893C

Test Material: SC-0224 (56.2% purity); Lot #EHC-0355-25. Note: Technical grade sulfosate is usually supplied as an aqueous solution. Because its viscous nature 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  $\leq 30\%$ ). From 1982 to the present time, the studies submitted to support registration had different a.i. contents ranging from 19.2 to 72%.

Synonyms: Trimethylsulfonium carboxymethylaminomethylphosphonate; sulfosate; Touchdown

Sponsor: Stauffer Chemical Co.

Study Number(s): T-11052

Testing Facility: Stauffer Chemical Co., Environmental Health Center, Farmington, CN

Title of Report: A Teratology Study in New Zealand White Rabbits with SC-0224.

Author(s): J. L. Minor and J. R. Downs

Report Issued: June 21, 1983

Conclusions: Sulfosate was administered by gavage to groups of mated New Zealand White rabbits (21 does in the highest dose group) on gestation days 7 through 19 at dose levels of 0, 10, 40, or 100 mg/kg/day. The test material was dissolved in water and administered in a volume of 2 ml/kg.

The maternal NOEL is 40 mg/kg/day according to the report, and the maternal LOEL is 100 mg/kg/day (6 deaths in 17 pregnant does, 4 abortions in the 11 survivors along with decreased body weight, feed consumption and body weight gain).

The developmental NOEL is 40 mg/kg/day and the LOEL is 100 mg/kg/day. This is based on the following: at 100 mg/kg/day, there was a reduction in the number of live fetuses/doe for the 7 surviving rabbits when compared with the controls (5.4 versus 7.4), 4 rabbits aborted their litters (apparently all of the fetuses were dead in those litters and if those are included in the calculations there would be a statistically significant decrease in live fetuses/doe and postimplantation loss), and having only 7 litters does not give a sufficiently high number of animals to absolutely conclude that no developmental toxicity is occurring, particularly in light of the massive losses to death and abortions.

Core Classification: Minimum.

This study satisfies the guideline requirements (§83-3) for a developmental toxicity study in rabbits.

Discussion: The original DER cited the increased incidence of clinical signs in the low dose group as the basis for setting the NOEL < 10 mg/kg/day (lowest dose tested). However, incidences reported (see table below, taken from Table 2 of the original report) indicate that those signs do not occur in a dose-related manner or in numbers that exceed control group values. It should also be noted that 4 of the 8 reported deaths appeared to be associated with dosing accidents (see attached Table 3 from the original report).

Attached Table 5 from the original report and the tables below summarize the effects of the test compound on body weight, weight change, and food consumption, and in utero results are summarized in the table below and in Table 7 in the Appendix.

All of these data suggest a maternal NOEL of 40 mg/kg/day and an LOEL of 100 mg/kg/day.

Data summarized in attached Tables 8, 9 and 10 from the original report indicate that possible developmental toxicity was observed at the highest dose tested (100 mg/kg/day).

# Clinical Signs for Does Gravid on Day 30

	Dose Levels (mg/kg/day)			
	0	10 <sup>a</sup>	40	100
<u>Females Examined</u>	14	14	14	7
Without signs	13	7*	10	4
<u>General</u>				
Anorexia	0	0	1	2
Diarrhea	0	1	2	2
Lethargy	0	0	1	1
Head tilt	0	1	0	0
Nasal discharge after dosing	0	1	0	0
Wet stains, chin	0	1	0	0
Scab, mouth	0	1	0	0
Red urine	0	1	0	0
Red stains on cage pad	0	1	1	0
<u>Respiratory</u>				
Rales while dosing	1	0	0	0

\*p ≤ 0.05

<sup>a</sup>Each one of the clinical signs was observed in a different animal. No one animal in the 10 mg/kg/day dose group had more than 1 clinical sign.

## Body Weight Gains (Kg)<sup>a</sup>

Group:	Prior to Dosing Period	Days 7 - 21	Days 21-30	Days 7 - 30	Corrected Body Weight Gain <sup>1</sup>
Control	0.3	0.2	0.0	0.2	-0.2
LDT	0.3	0.1	0.1	0.1	-0.3
MDT	0.3	0.1	0.1	0.2	-0.3
HDT	0.4	-0.3*	0.3*	0.0*	-0.4

<sup>1</sup>corrected body weight gain for entire gestation period = body weight gain for days 7 - 30 minus gravid uterus weight.

<sup>a</sup>Data extracted from table 5.

\* p < 0.05

## Food Consumption Data (g/day)<sup>a</sup>

Group:	Days 0 - 7	Days 7 - 21	Days 21 - 30	Days 7 - 30
Control	190	165	104	3200
LDT	191	136	119	2600
MDT	174	136	134	3000
HDT	199	54*	180	2000*

<sup>a</sup>Data extracted from table 5.

\* p < 0.05

# Cesarean Section Observations<sup>a</sup>

	Control	LDT	MDT	HDT
Dose (mg/kg/day)	0	10	40	100
# Animals Assigned	15	15	15	21
# Animals Mated/Inseminated	15	15	15	15
Pregnancy Rate (%)	14(93)	14(93)	14(93)	17(81)
Maternal Wastage				
# Died	0	0	0	8* <sup>b</sup>
# Died/pregnant	0	0	0	6
# Non pregnant	1	1	1	4
# Aborted	0	0	0	4*
# Dams with live fetuses	14	13	14	7
Total Corpora Lutea	119	132	113	73 <sup>c</sup>
Corpora Lutea/dam	8.5	9.4	8.1	8.0
Total Implantation	117	103	104	133 <sup>d</sup>
Implantations/Dam	8.4	7.4	7.4	7.1 <sup>d</sup>
Total Live Fetuses	103	86	100	38
Live Fetuses/Dam	7.4	6.6	7.2	5.4 <sup>d</sup>
Total Resorptions	14	17	4	12
Early	8	3	3	6
Mid	3	1	0	1
Late	3	13	1	5
Resorptions/Dam	1.0	1.3	0.3	1.7
Total Dead Fetuses	0	0	0	0
Dead Fetuses/Dam	0	0	0	0
Mean Fetal Weight (gm)	43	47	46	48
Preimplantation Loss(%)	2	22*	6	9
Postimplantation Loss(%)	12	6	4	22 <sup>d</sup>
Standard Deviation	13	9	6	20
Sex Ratio (% Female)	56	60	56	61

<sup>a</sup>Data extracted from table 7.

\* p < 0.05

<sup>b</sup>4 of 8 deaths were from dosing accidents.

<sup>c</sup>Some of these data were not available.

<sup>d</sup>Implantation sites were found in 17 dams. Later, only 7 dams had litters to term. If the values include the 4 females which aborted, then the following would values would be used:  
implants/dam -  $7.6 \pm 1.6$ , live fetuses/dam -  $3.4* \pm 3.0$  and  
postimplantation loss (%) -  $49* \pm 42$ .

## Substantive Review

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