

011337

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DATA EVALUATION RECORD  
(Addendum of June 3, 1993)

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

EPA Identification No.s: EPA Accession No. 249802  
EPA Pesticide Chemical Code: 128501  
Toxicology Chemical Code: 893C

Test Material: SC-0224 (19.2% purity); Lot #EHC-0355-25

Synonyms: Trimethylsulfonium carboxymethylaminomethylphosphonate;  
sulfosate; Touchdown

Sponsor: Stauffer Chemical Co.

Study Number(s): T-11050

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

Title of Report: A Teratology Study in CD® Rats with SC-0224.

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

Report Issued: November 5, 1982

Conclusions: Sulfosate was administered by gavage to groups of pregnant Sprague-Dawley rats on gestation days 6 through 20 at dose levels of 0, 30, 100, or 333 mg/kg/day. The test material was dissolved in water and administered in a volume of 5 ml/kg.

The maternal NOEL is 100 mg/kg/day, and the maternal LOEL is 333 mg/kg/day (undetermined death of 2 dams, decreased body weight, feed consumption and body weight gain along with increased incidences of salivation, chromorhinorrhea, and lethargy after dosing).

The developmental toxicity NOEL is 100 mg/kg/day, and the developmental LOEL is 333 mg/kg/day (decreased fetal body weight).

Core Classification: Minimum. (NOTE: This study was originally classified as core supplementary because of a question regarding determination of the doses administered in terms of the active ingredient or the test substance which contained 19.2% active ingredient. A laboratory audit report verified that the doses

were based on the amount of active ingredient administered, and the study was upgraded from supplementary to minimum. 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%).

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

Discussion: The report and original DER noted significant reductions in body weight and feed consumption at the highest dose level (333 mg/kg/day) along with increased incidences of dams with salivation, lethargy after dosing, and chromorhinorrhea. Selected clinical signs, body weight and body weight gain and food consumption data are summarized in the following tables:

Summary of Clinical Signs in Dams				
Dose (mg/kg/day)	0	30	100	300
No. examined	24	24	22	20
Chromorhinorrhea	2	2	2	9*
Salivation	0	0	0	7*
Lethargic after dosing	0	0	0	8*

\* Statistically significantly different from control value,  $p \leq 0.05$ , Mann-Whitney U test.

Summary of Body Weight and Body Weight Gain (g)<sup>a</sup>

		Dose Level (mg/kg/day)			
		0	30	100	333
Pregnant Survivors		24	24	22	20
Body Weight (g)					
Day					
0		234	238	234	234
6		266	268	266	268
9		271	272	274	252*
12		289	292	289	266*
16		314	320	306	277*
21		387	386	370	322*
Body Weight Gain (g)					
Days					
6-9		5	3	8	-15*
6-12		23	24	23	-2*
12-16		25	28	17	11*
6-16		48	52	40	9*
16-21		73	66	64	45*
Uterine Weight		91	89	82	74
Net Body Weight Change		29	29	22	-19*

<sup>a</sup>Extracted from Table 5 of study.

\*Statistically significant ( $p < 0.05$ )

	Food Intake (g/day) <sup>a</sup>			
	0 mg/kg	30 mg/kg	100 mg/kg	333 mg/kg
Day				
0-6	23	22	23	23
6-9	24	22	21	9*
9-12	24	25	22	12*
12-16	26	26	24	15*
16-21	27	28	25	18*

<sup>a</sup>Extracted from Table 5 of study.

\*  $p < 0.05$

Based on these results plus the undetermined death of 2 dams at the high dose, the maternal NOEL is 100 mg/kg/day, and the maternal LOEL is 333 mg/kg/day (decreased body weight, feed consumption and body weight gain along with increased incidences of salivation, chromorhinorrhea, and lethargy after dosing).

The only developmental toxicity noted in the report was decreased fetal weights at the 333 mg/kg/day dose level, and the original DER reported increases (not statistically significantly increased in comparison to the control group value) in the number of early resorptions per dam at the 100 and 333 mg/kg/day dose levels. In utero results are also summarized in the attached copy of Tables 5, 6, 7 and 8 from the report.

The increases in resorptions at the mid and high dose levels are not toxicologically significant because:

- (1) There were no significant differences in group mean litter sizes,
- (2) There were no statistically significant differences noted between the control and each of the treated groups (statistics were conducted on % resorptions, not on total resorptions/dam). The standard deviations for all groups, including controls were larger than the means.
- (3) In examining the individual litter data for the early resorptions, it is noted that in both the mid- and high dose groups, there were 1 or 2 outliers. In the high dose group, 1 dam had 11/14 early resorptions/implantations and 2 had 3 (3/12 and 3/15). The rest had 2, 1 and 0. In the mid-dose group, 1 dam had 7/14 early resorptions and 1 had 3/17. The rest had 2, 1 and 0. In the low dose group, 2 had 3 (3/11 and 3/13) and the rest had either 2, 1 or 0 early resorptions and in the control group, they all had either 2, 1 or 0 resorptions.

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

	Control	LDT	MDT	HDT
Dose (mg/kg/day):	0	30	100	333
# Animals Assigned	25	25	25	26
# Animals Mated/Inseminated	24	24	22	23
Pregnancy Rate (%)	96	96	88	88
Maternal Wastage				
# Died	0	0	0	3
# Died/Pregnant	0	0	0	3 <sup>b</sup>
# Non Pregnant	1	1	3	3
# Aborted	0	0	0	0
# Premature Delivery	0	0	0	0
Total Corpora Lutea	365	384	329	306
Corpora Lutea/Dam	15.2	16.0	15.0	15.3
Total Implantations	337	345	299	304
Implantations/Dam	14.0	14.4	13.6	14.5
Total Live Fetuses	318	323	275	277
Total Dead Fetuses	0	1	1	1
Live Fetuses (%)	94	96	91	88
Dead Fetuses (%)	0	0.3	0.3	0.4
Total Resorptions	19	21	23	26
Early (%)	4.3	5.6	7.7	9.0
Mid (%)	0.9	0	0	2.0
Late (%)	0.5	0.3	0.9	0
Resorptions/Dam	0.79	0.88	1.05	1.3
Live Litters				
Live Fetuses/Dam	13.3	13.5	12.5	12.8
Dead Fetuses/Dam	0	0.04	0.05	0.05
Mean Fetal Weight (gm)	5.0	4.9	4.9	4.2*
Sex Ratio (% Female)	51	53	50	48

<sup>a</sup>Data extracted from tables 2 and 5

\* p < 0.05

Based on these results, the developmental toxicity NOEL is 100 mg/kg/day, and the developmental LOEL is 333 mg/kg/day (decreased fetal body weight).

Substantive Review

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