Study No.
T-7098.2; ST54
Oral Toxicity Rangefinder for Perfluorooctane Sulfonyl Fluoride (POSF) in Rats

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Study Objective

The research objective of this study was to provide preliminary data to characterize the toxicity of perfluorooctanesulfonyl fluoride (POSF) following a single oral exposure in rats.

Method Summary

This study was performed in the 3M Strategic Toxicology Laboratory under a defined protocol (1) and classified as a "Class B Study" as explained in TOX SOP 0950, Strategic Toxicology Lab GLP Program Procedure (2).

POSF was administered to male rats at dose levels of 100, 300 and 600 mg/kg body weight (N=1 per dose level) using a dosage volume of 5 ml suspension / kg body weight. A uniform suspension was prepared in 2% Tween 80 immediately prior to dosing. Re-suspension of solids was performed with 5 strokes of the tissue grinder pestle before the sample was drawn-up in the syringe for dosing. A vehicle control animal received 2% Tween 80 at a dose volume of 5 ml/kg. This animal, however, was humanely sacrificed on day one post-dose in order to obtain liver tissues for histological comparison in another study. A second group of age-matched control animals (N=3) were treated with propylene glycol at a dose volume of 5ml/kg body weight and were used for weight gain comparison purposes. This second group of control animals was shared between this study and T-7585.1, T-7576.1, T-7574.1, T-7575.1, T-7576.1, and T-7577.1. Historical toxicity data on these two vehicle control substances indicate that substitution of propylene glycol for 2% Tween 80 would not significantly effect the results of the endpoints monitored in this study. All animals were monitored for morbidity, mortality, and bodyweight changes for two weeks following dosing, and were then humanely euthanized.

Results and Discussion

All POSF dosed animals survived to the end of the two-week study period and gained an average of 53 ± 0.18 grams of body weight. From day 2-post dose through the end of the 14-day study period, the rate of weight gain was comparable to the propylene glycol vehicle control animals. Transient weight loss was observed in the animals dosed with 300 mg/kg POSF on day-one post dose. Treatment group results are shown in Table 1. All propylene glycol treated vehicle control animals survived to the end of the two-week study period, and gained an average of 50 ± 0.16 grams, or 16 percent of their average initial body weight. The results of the control group are shown in Table 2.

The dose levels of POSF were chosen in order to compare the relative oral toxicity of POSF the known oral LD50 of perfluorooctanesulfonate (PFOS), which is 251 mg/kg in male rats (3). The hypothesis has been put forth that toxicity resulting from POSF exposure can be attributed to the PFOS exposure resulting from absorption and hydrolysis of POSF to PFOS following oral dosing. In a previous study on the toxickokinetics of POSF in rats (T-7098.1), rats were dosed by oral gavage with 5 mg/kg of POSF. On day one post-dose, approximately 5% of the POSF dosed was present in the liver, and on day 4 post-dose, approximately 11% of the dose was found as PFOS in the liver. Very little PFOS was found in the serum, only about 0.1% of the POSF

dosed on days 1 or 4 respectively. Assuming that only ten percent of the dose of POSF is available to the liver as PFOS, that 25% of the dose is available following a similar oral dose of PFOS, and that toxicity resulting from POSF exposure can be attributed to the resulting PFOS exposure, the predicted oral LD50 of POSF would be approximately 2.5 times higher than that of PFOS. Based on these assumptions, the 600 mg/kg dose of POSF used in this study was not high enough to determine whether the toxicity resulting from POSF exposure can be attributed to the resulting PFOS exposure. In order to investigate this hypothesis, a dose of at least 628 mg/kg POSF would be needed.

Conclusions

The results of this study indicate that the POSF is not acutely toxic to male rats at oral doses less than or equal to 600 mg/kg body weight (N=1/dose group), under the conditions used in this study.

List of Tables

Table 1: Treatment Group Results - POSF Oral Toxicity Rangefinder

			Body Weight (g)						Body Weight Gain (g)					
Animal #	Sex	Dose (mg/kg) / date	day 0	day 1 PD	Day 3 PD	Day 4 PD	Day 7 PD	Day 14 PD	Day 0-1 PD	Day 1-3 PD	Day 3-4 PD	Day 4-7 PD	Day 7-14 PD	Day 0-14 PD
1R00165	M	100 / 1-22-01	287	287	297	303	319	342	0	10	6	16	23	55
1R00166	M	300 / 1-22-01	285	277	287	295	313	343	-8	10	8	18	30	58
1R00167	M	600 / 1-22-01	282	285	291	293	306	328	3	6	2	13	22	46

Table 2: Control Group Results - POSF Oral Toxicity Rangefinder

			Body Weight (g)				Body Weight Gain (g)			
Animal #	Sex	date of dosing	day 0	day 2 PD	Day 7 PD	Day 14 PD	Day 0-2 PD	Day 2-7 PD	Day 7-14 PD	Day 0-14 PD
1R00184*	M	01/29/2001	310	324	337	362	14	13	25	52
1R00185*	M	01/29/2001	293	303	316	343	10	13	27	50
1R00186*	M	01/29/2001	318	327	335	365	9	8	30	47

* Control animals also used in studies ST55 & ST65; dosed with 5ml/kg propylene glycol

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References

1) 3M Medical Department, Corporate Toxicology Protocol for Study No. T-7098.2; ST54 Oral Toxicity Rangefinder for Perfluorooctane Sulfonyl Fluoride (POSF) in Rats, January 2001.

2) 3M Medical Department, Corporate Toxicology Strategic Toxicology Laboratory Standard Operating Procedure (TOX SOP) No. 0950 – GLP Program Procedure, 1999.

3) Dean, W.P., Jessup. D.C- Thompson, G., Romig, G. and Powell, D. 1978. Fluorad® Fluorochemical Surfactant FC-95 acute oral toxicity (LD50) study in rats. Report No. 137-083. International Research and Development Corporation, Mattawan. MI.