# SIDS INITIAL ASSESSMENT PROFILE

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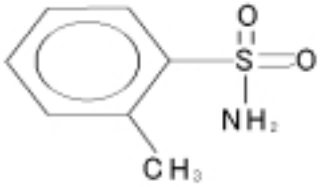
| **CAS No.** | 88-19-7 |
| **Chemical Name** | *o*-Toluenesulfonamide |
| **Structural Formula** |  |

## RECOMMENDATIONS

The chemical is currently of low priority for further work.

## SUMMARY CONCLUSIONS OF THE SIAR

### Human Health

o-Toluenesulfonamide orally administered was rapidly eliminated mostly to urine in rats. In human subjects it was excreted to urine more slowly than that in rats. The main metabolites were 2-sulfamoyl-benzyl alcohol and its sulphate and glucuronic acid conjugates in both rats and humans. Saccharin was also detected as a metabolite in urine especially in humans.

The oral $LD_{50}$ value for rats was greater than 2,000 mg/kg b.w. in males and between 1,000 and 2,000 mg/kg b.w. in females [OECD TG 401]. Sedation, passivity and catalepsy appeared even at the lowest dose of 700 mg/kg b.w. It is reported that this chemical was moderately irritating to eyes in rabbits but the reliability of the study is uncertain. There is no available information on skin irritation and sensitization.

In accordance with an OECD combined repeated dose and reproductive/developmental toxicity screening test [TG 422], o-toluenesulfonamide was given to male and female SD rats by gavage at 0, 20, 100, 500 mg/kg b.w./day for at least 38 days. Three females died and two females were sacrificed in moribund condition during the pre-mating period at 500 mg/kg b.w. Decreased locomotor activity and appearance of prone position and salivation were observed in both sexes at 100 and 500 mg/kg b.w. In the same groups, low body weights were recorded in both sexes. In histopathological examinations, hypertrophy of the centrilobular hepatocytes with the cytoplasm having a ground glass appearance was observed in both sexes at 100 and 500 mg/kg b.w. in a dose-dependent manner. In addition, the incidence of fibrosis and cellular infiltration of the pericardium, and fibrosis and cellular infiltration of the capsule and atrophy of the thymus were significantly increased in females of at 500 mg/kg b.w.. In the kidneys, eosinophilic body was observed in males of all treated groups, maybe due to the complex accumulation of this chemical with the male rat specific protein, alpha-2u-globulin. Based on clinical signs and hepatic change, the NOAEL for repeated dose toxicity is considered to be 20 mg/kg b.w./day for both sexes.

Regarding genotoxicity, a bacterial test [OECD TG 471] and a chromosomal aberration test [OECD TG 473] *in vitro* were negative with and without metabolic activation. One mammalian spot test in mice demonstrated inconclusive results and two micronucleus tests *in vivo* in mice (gavage and i.p.) showed negative results. However the experimental condition of all these studies are not sufficiently reported. Therefore, the genotoxic potential of

this chemical *in vivo* is inconclusive.

In a two generation lifetime feeding study, male and female SD rats were given o-toluenesulfonamide in the diets at 0, 2.5, 25 and 250 mg/kg b.w./day. No increase in any tumour incidence was noted in all dose groups of both generations. Two 2-year oral rat studies also demonstrated no carcinogenicity of this chemical. Only one lifetime feeding study showed low incidence of urinary bladder tumors of rats but the reliability of this study is uncertain because of poor reporting. A cell transformation assay using mammalian cultured cells showed negative results. Based on a weight of evidence approach, the available data indicates that this chemical is not carcinogenic.

In an OECD combined repeated dose and reproductive/developmental toxicity screening test [TG 422], a significant reduction in body weights of pups was observed on days 0 and 4 in both sexes of rats at 500 mg/kg b.w. In a two generation lifetime feeding study, decrease of litter size and pup body weight was observed at 250 mg/kg b.w./day. Based on an overall evaluation of both results, the appropriate NOAEL for reproductive/developmental toxicity is considered to be 100 mg/kg b.w./day .

**Environment**

*o*-Toluenesulfonamide is soluble in water (1.6 g/L at 25 °C) and has a low vapor pressure ($6.6 \times 10^{-5}$ Pa at 25 °C) Its log Kow is 0.84. *o*-Toluenesulfonamide is not readily biodegradable (OECD TG301C: 0 % by BOD after 14 days), but its experimental BCF of less than 2.6 (OECD TG 305) suggests that this chemical does not bioaccumulate in aquatic organisms. Hydrolysis is not expected to occur. If released to the atmosphere, this chemical mainly exists in the particulate phase according to its low vapor pressure. Particulate phase of *o*-Toluenesulfonamide may be physically removed from the air by dry and wet deposition.

Acute toxicty of o-Toluenesulfonamide has been tested in three aquatic species of three trophic levels. For algae (*Selenastrum capricornutum*) a ErC50 of 170 mg/L (OECD TG 201, growth rate for 24-48hr and also 24-72 h) and a 72hEbC50 of 57 mg/L (OECD TG201, biomass) were determined. For daphnids (*Daphnia magna*) a 48 h EC50 of 210 mg/L (OECD TG 202 part 1), and for fish (*Oryzias latipes*) a 96 h LC50 of >100 mg/L (OECD TG 203) were reported.

Two chronic toxicity values, for alga (*Selenastrum capricornutum*) and daphnids (*Daphnia magna*) were available. For algae, a 72 h NOEC on growth inhibition of 7.7 mg/L(OECD TG 201, based on growth rate), and for daphnids, a 21 d NOEC of 49 mg/L(OECD TG 202, reproduction) were reported.

**Exposure**

*o*-Toluenesulfonamide was mainly produced as a chemical intermediate for the production of saccharin in the past, but now saccharin is normally manufactured without using this chemical although minor amounts are still used for this purpose. A mixture of *o*-Toluenesulfonamide with the *p*-isomer is used as a plasticizer for hot-melt adhesives, a chemical intermediate for fluorescent pigments and a chemical intermediate for plasticizer resins. The production volume of this chemical in Japan was about 50 tonnes in 2000.

## NATURE OF FURTHER WORK RECOMMENDED

This chemical is not a candidate for further work because all SIDS endpoints are sufficient.