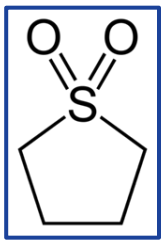
SUMMARY

Background: Sulfolane is a chemical used to separate components of a mixture, especially in natural gas and oil petroleum refineries. Sulfolane has been found in groundwater and drinking water wells near some refineries, and humans may be exposed through contaminated drinking water. The effects of exposure to sulfolane in drinking water were studied in male and female rats (starting in utero) and male and female mice (starting in adolescence) to identify potential toxicity or cancer-related outcomes.



Methods: Pregnant rats were given sulfolane in drinking water at 30, 100, 300, or 1,000 milligrams (mg)/liter (L) throughout pregnancy and nursing of their offspring. Afterwards, groups of 50 male and 50 female offspring continued the same exposures as their mothers for 2 years. Fifty male and 50 female mice were given sulfolane in drinking water at 30, 100, 300, or 1,000 mg/L for 2 years beginning in adolescence. Control animals (rats and mice) were given drinking water alone with no chemical added (0 mg/L sulfolane). Ten male and female rats and five male and female mice per group were removed at 3 months for evaluation of organ weights, blood concentrations, clinical pathology (clinical measures in the blood), reproductive parameters, and the potential for sulfolane to damage DNA. At the end of each 2-year study, tissues from more than 40 sites from every animal were examined for signs of disease.

Results: Exposure of pregnant rats to sulfolane had no overt effect on their health and survival. However, rat offspring in the highest exposure group (i.e., 1,000 mg/L) had reduced body weight during nursing. Decreased body weights persisted in female rats until 2 years of age. In female rat offspring, vaginal opening (an important developmental marker of puberty) was delayed in the 300 and 1,000 mg/L groups. Water consumption was decreased in the highest exposure group in both male and female rats. In female rats exposed to 1,000 mg/L for 2 years, neoplasms (which can include benign or malignant growths) were observed in the mammary gland. Exposure of mice to sulfolane had no overt effect on their health and survival, and no effects on body weight were observed. In mice exposed to sulfolane for 2 years, neoplasms were observed in the liver of females in the 1,000 mg/L group. Hemangiosarcoma (a malignant cancer related to blood vessels) was increased in male mice in the 1,000 mg/L group. Other effects observed in mice exposed to sulfolane included noncancerous tissue abnormalities in the liver of males and females and in the ovary of females. Tests to evaluate the potential for sulfolane to damage DNA were negative.

Conclusions: *The NTP four-point scale rates the level of evidence that a substance has the ability to cause cancer in laboratory animals. Under the conditions of these 2-year drinking water studies, there was clear evidence that sulfolane exposure has the ability to cause cancer based on the hemangiosarcoma in all organs, predominately the liver, in male mice. There was equivocal (uncertain) evidence that it has the ability to cause cancer in female mice based on liver neoplasms and mammary neoplasms in female rats. There was no evidence that it has the ability to cause cancer in male rats. In addition, sulfolane exposure caused increased incidences of noncancerous tissue abnormalities in the liver in male and female mice and the ovary in female mice. Sulfolane exposure also caused a delay in vaginal opening in female rats.*