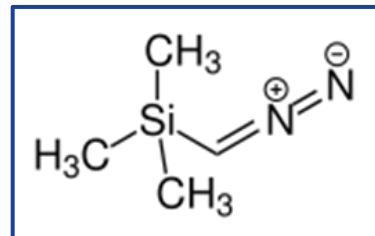


SUMMARY

Background: Trimethylsilyldiazomethane (TMSD) is a commercially available chemical used in laboratories. It has been considered a safer alternative to the related compound diazomethane, which causes lethal lung injury in both humans and animals. TMSD was selected for study because accidental workplace inhalation exposure resulted in the death of two chemists, and there was a lack of toxicity data to support the claim that it is safer than diazomethane. The effects of inhaled TMSD in male rats and mice were studied to identify potential toxicity that could be relevant to humans.



Methods: Groups of eight male rats and mice were exposed by inhalation to TMSD vapors at 10 parts per million (ppm) for 30 minutes for 1 day or at 0.3, 1, 3, or 10 ppm for 30 minutes per day for 5 days. The animals were either euthanized the day after the last exposure or held for 5 or 9 days to assess recovery and any delayed effects. Control animals were exposed to air alone, with no TMSD added (0 ppm). Body weight measurements and clinical observations were taken during the study. Tissues from more than 40 sites from every animal were examined for signs of toxicity.

Results: Rats in all exposure groups survived. However, five out of eight mice in the 1-day exposure group held for 9 days and all mice in the 5-day 10 ppm exposure groups died or were euthanized due to illness before the end of the study. The major findings for rats and mice in the highest exposure groups included labored breathing, increased lung weight, injury, inflammation, scarring, bleeding, and accumulation of fluid in the lungs relative to unexposed control animals.

Conclusions: Under the conditions of these 1-day and 5-day studies, exposure to TMSD by inhalation caused acute and progressive damage to the lungs of rats and mice, and these effects occurred after a single 30-minute exposure to the chemical. These data provide useful information about potential hazards of TMSD exposure in the workplace and alert chemical suppliers to those dangers.
