SIDS INITIAL ASSESSMENT PROFILE

CAS No.	127-19-5
Chemical Name	N,N-Dimethylacetamide (DMAC)
Structural Formula	$CH_3CON(CH_3)_2$

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

DMAC is well-absorbed orally, by inhalation and dermally. There are adequate data with which to evaluate the potential hazard to human health of this compound. DMAC has low toxicity by ingestion: the oral LD 50 ranges from 3000 mg/kg bw to 6000 mg/ Kg in rats and > 5000 mg/Kg bw in rabbits. The chemical is harmful by dermal route and inhalation: dermal LD 50 values were 7500 mg/kg bw in rats, 9600 mg/Kg bw in mice, from 2100 mg/kg bw to 3600 mg/Kg bw in rabbits, but less than 940 mg/ kg bw in guinea pig. Inhalation LC 50 rat was 8.81 mg/l, 1h (˜ 2.2 mg/l, 4h) and LC 50 mouse was 1.47 mg/l, 3.5 h. DMAC is not a skin sensitiser or skin irritant and was only slightly irritating to the eyes. In repeated dose studies (14 days to 2 years) NOAECs of 25 ppm (0.09 mg/l) and higher have been observed in inhalation studies with rats and mice. Effects observed included liver degeneration, some irritation to the respiratory tract and decreased body weight gain. A NOAEL oral of 300 mg/Kg, 24 months, has been observed in oral studies with rats. Observation included kidney and adrenal weights. DMAC does not show mutagenic effects in several *in vitro* and *in vivo* tests. UDS in human diploide fibroblast and a transgenic mouse mutation assay on liver tissue are negative. For the *in vivo* tests two dominant lethal assays with rat (dermal and inhalation) were negative and dominant lethal assays on mouse (dermal, inhalation and i.p.) were negative too. A cytogenetic assay on human lymphocytes from 20 workers who were in contact with DMAC didn't reveal an increase in the frequency of chromosome aberration. DMAC was not carcinogenic in a two year drinking water study and a two year inhalation study in rats and to an 18 months inhalation study in mice. DMAC has been extensively studied for reproductive toxicity properties. Fertility was not affected when male rats had been exposed to up to 386 ppm (1.4 mg/l) in a 43 days inhalation study and in a 10 weeks one-generation inhalation study up to 300 ppm (1.08 mg/l) (females also were exposed). No effects in mice were observed in a sperm abnormalities test with exposures up to 700 ppm (2.52mg/l)for 6 weeks. Developmental toxicity was also investigated: the inhalation study in rats showed no adverse effects at the highest concentration, 300 ppm (1.08 mg/l), other than reduced maternal and fetal weight. The rabbit inhalation study showed a small increase in cardiac malformations at 570 ppm (2.052mg/L), in absence of maternal toxicity signs. The oral studies (rat and rabbit) indicate that high doses can cause both maternal and embryofetal toxicity. In an oral study on rat at 65, 160, 400 mg/kg bw/day the highest dose of DMAC was able to induce specific teratogenic effects such as great vessel malformations and anasarca at maternal toxic levels and the NOEL is 160 mg/kg bw/day. These findings were confirmed by a second oral study on rat performed at the same dose levels, from which a NOEL of 65 mg/kg bw/day can be derived. Due to the observed signs of specific developmental toxicity DMAC has to be considered a developmental toxicant.

Effects seen in the dermal studies (rat and rabbit) occurred at high and generally maternotoxic doses. A recent *in vitro* embryotoxicity study has been performed and embryotoxicity and teratogenic effects were observed at the highest levels. A NOEC was derived, corresponding to an *in vivo* NOEL of 100 ppm as the concentration in the

plasma after the exposure to 100 ppm in air in another study, may be similar to the NOEL observed in this study. Liver impairment was observed in 19 out of 41 workers who had been working from 2 to 10 years in a spinning unit (airborne levels were not reported). Upper respiratory tract, gastric and nervous disturbances were complained. Biological monitoring of workers exposed to DMAC in an acrylic fibre plant was performed: brief threshold limit value-level exposures and chronic low level exposure do not cause hepatotoxic clinical chemistry responses. A retrospective epidemiologic study was undertaken in 571 workers with a 12-months simultaneous exposure to acrylonitrile and no relationship between tumors and DMAC exposure was found. Also dermal absorption and inhalation of DMAC in human volunteers was carried out. They were exposed twice to DMAC for 4 h at intervals of 96 h or above to 6.1 ppm). Mean dermal absorption was estimated to be 40.4% of the total DMAC uptake. DMAC vapour was significantly absorbed through the skin. Biological half lives of urinary MMAC were 9h for skin and 5.6 h for lung respectively.

Environment

Releases of DMAC to the environment are to be expected with waste water (treated), solid wastes (incinerated), exhaust gas (in air by vent), and a residue in the raw acrylic fibres is < 0.5% by weight and in the raw elastane yarns from 0.1% to 3% by weight. DMAC has been tested in aquatic species: alga *Scenedesmus* 72 h -EC50 > 500 mg/l; daphnia 48 h- EC 50 > 500 mg/l, fish acute toxicity 96 h- LD 50 > 500 mg/l. A NOEC for *Daphnia* at 48 h is 1000 mg/l and for *Mysidopsis bahia* a NOEC at 96 h is 320 mg/l. Therefore DMAC is not acutely toxic to aquatic organisms. From the EC50 value for alga *Scenedesmus* of 500 mg/l a $PNEC_{aqua}$ of 0.5 mg/l can be derived by applying an assessment factor of 1000. This factor is justified as long term effect values are not available.

Exposure

The worldwide production volume of Dimethylacetamide in the year 2000 is estimated to be from 50000 to 60000 tons/ year. The substance is mainly used for polymer dissolution in the man-made fibre production industry. It is produced in closed system and processed at the production sites (non dispersive use). DMAC production is limited to the replacement of losses occurring during the production, processing and recovery. DMAC is also used in fine chemical industry. It is not intended to be used by the general public. DMAC is a colourless liquid, completely miscible with water, with a vapour pressure of 1.76 hPa at 20°C. It doesn't hydrolyse and undergoes photochemical degradation with half-life time of 6.1 hours. A bioconcentration factor (BCF) of 0.008, calculated from log octanol-water partition coefficient (log Kow) of –0.77, indicates a low bioaccumulation potential in aquatic species. A low adsorption to soils and sediments can be assumed by a calculated Koc of 9.1. DMAC is inherently biodegradable (77-83 % after 14 days). Distribution MacKay model indicates that considering a release of DMAC into the air, it is likely to be transported in water and soil.

Occupational exposure may occur through dermal contact and vapour inhalation during the use of DMAC. No exposure is envisaged during production and recovery of DMAC as this takes place in a closed system. An air extraction equipment placed above the processing units was adopted to limit any exposure and workers wear solvent-proof gloves during some critical operations, such as fibre spinning, so significant exposure is not expected.

Consumer exposure is negligible as results from migration tests with simulated sweating on textile articles containing residual DMAC (from 0.01% to 0.001%).

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.