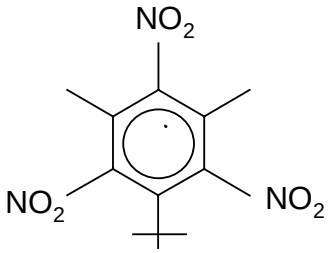
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	81-15-2
Chemical Name	1-tert-butyl-3,5-dimethyl-2,4,6-trinitrobenzene (Musk xylene)
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work for the environment and human health.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The acute oral LD_{50} in mice and rats was established at >2000 mg/kg bw. In a limited dermal study an application of 10000 or 15000 mg/kg bw caused no mortality in groups of three rabbits. The dermal test is not performed according to current standards. However, it is expected that the acute dermal toxicity is >2000 mg/kg bw. Data for acute inhalation toxicity were not available.

Musk xylene is not considered to be irritating for skin and eyes and is not a skin sensitiser. For respiratory tract irritation no data are available.

In a 90-dermal study with rat a NOAEL of 24 mg/kg bw was derived. Increased liver weight was observed at higher doses.

Musk xylene was negative in several *in vitro* tests (bacterial gene mutation tests, SOS-chromosome aberration test, mammalian gene mutation test, tests for chromosome aberrations and SCEs in mammalian cells, a micronucleus test in mammalian cells and an UDS test). In an *in vivo-in vitro* rat hepatocyte UDS test also negative results were obtained. Musk xylene is not-genotoxic.

Musk xylene is considered to be a carcinogen in mice acting by a non-genotoxic mode of action. The only tumours reported were liver carcinomas (malignant) in B6C3F1 mice, a mouse strain prone to develop this kind of tumours, and benign malformations in the Harderian gland. The latter type of tissue does not occur in humans and therefore these benign tumours are difficult to interpret with respect to their relevance to humans. It is concluded that there is limited evidence for carcinogenicity of musk xylene in animals as was also stated by IARC.

With respect to fertility no generation study was available for either route. However in a 90-day dermal toxicity study with rats and also in an oral carcinogenicity study with mice musk xylene caused no effects on the reproductive

organs. In a peri/post natal study no effects on sexual development and fertility were reported in pups which were exposed *in utero* and during lactation. A peri/postnatal study was performed, in which the F_1-generation was exposed to musk xylene *in utero* or through any transfer in the milk of the lactating dams. Slight pup toxicity, reflected in a reduced but statistically not significant body weight gain, was observed at the highest dose level. In this study 7.5 mg/kg bw/day could be considered as the NOEL for peri/postnatal effects.

In an oral developmental study with rats maternal toxicity, expressed as decreased body weight gain and food consumption, was seen in the mid and high dose level of 60 and 200 mg musk xylene/kg bw/day. Embryo toxicity (extra thoracic ribs and increased ossification) was seen at the highest dose level tested. The NOAEL for maternal toxicity in this study can be established at 20 mg/kg bw/day and the NOAEL for developmental toxicity at 60 mg/kg bw/day. There is no indication for teratogenicity.

The available data obtained from the peri/post natal study indicate that musk xylene can be secreted into the milk into sufficient quantities to elicit toxic responses in the offspring of the test animals.

In a 90-day dermal toxicity study with rats, no indications for a neurotoxic potential were found for musk xylene.

Environment

EUSES (Simple Treat) estimates the following default distribution for musk xylene in an STP: air: 0%, water 43% and sludge: 57%. Based on the structure musk xylene is not expected to hydrolyse. Photodegradation has been demonstrated but is expected to be minimal in the aquatic environment. Musk xylene is not readily biodegradable. The measured BCF in bluegill sunfish is 4400 l/kg, which is in agreement with the calculated BCF based on log Kow.

The t (L)EC50 values for musk xylene were > 0.15, > 0.15 and 1.2 mg/l for algae, Daphnia and fish, respectively. NOEC values were derived for algae, daphnia and fish: > 0.56, 0.056 and 0.01 mg/l, respectively. In a 14-day acute toxicity study on earthworms no effects on survival up to the highest concentration of 50 mg/kg soil was observed. Musk xylene does not bind to the estrogen receptor in fish (*Oncorhynchus mykiss*) and clawed frog (*Xenopodus laevis*) *in vitro*. For the metabolites 2-amino musk xylene and 4-amino musk xylene binding in both species was observed. The relevance of these *in vitro* tests for the environment is still unclear.

Exposure

Musk xylene is a solid powder, with a melting point of 112-114 ^{o}C. The Log Kow is 4.9. Using a vapour pressure of 0.00003 Pa at 20 ^{o}C and a water solubility of 0.15 mg/l a Henry's law constant of 0.0595 Pa.m3/mol is calculated.

The use volume of musk xylene in 1998 in Europe is approximately 86 tonnes, including export to non-EU countries. The use volumes are decreasing. There is no production of musk xylene in the EU. Industry sources estimate that 20-30% of their products is exported outside the EU as finished fragrance compounds or in consumer products. Musk xylene can enter the aqueous and terrestrial environment via formulation sites and private use. The calculated exposure concentrations in air from formulation sites are minimal.

There is a potential for occupational and consumer exposure through inhalation and skin contact although exposures via inhalation are expected to be low due to the low vapour pressure. Consumer exposure to musk xylene will occur principally through its use in cosmetics. Indirect exposure via the environment is also possible.

NATURE OF FURTHER WORK RECOMMENDED

Sufficient information exists to address hazard classification for all SIDS endpoints and for other non-SIDS endpoints.

The chemical is a candidate for further work for the environment because:

- it is not readily biodegradable
- it has bioaccumulating potential (BCF = 4400 l/kg) and
- its long-term toxicity (NOEC < 1 mg/l)

The chemical is a candidate for further work for human health because:

- exposure via breast milk can occur
- the effects on pups in the peri/post natal study cannot be disregarded.

In view of these hazards, national or regional exposure information gathering and risk assessment may be considered.

The EU risk assessment is close to completion.