SIDS INITIAL ASSESSMENT PROFILE

CAS No.	106-99-0
Chemical Name	1,3-Butadiene
Structural Formula	CH_2=CH-CH=CH_2

CONCLUSIONS AND RECOMMENDATIONS

This chemical is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The total global production capacity of 1,3-butadiene is 1,202,000 - 4,960,000 tonnes/year. In Western Europe, 1,742,000 tonnes were produced in 1993 and 1,892,000 tonnes in 1994. This chemical is used as a monomer in the manufacture of a variety of synthetic rubbers and plastics (96%), or as an intermediate in the production of several other compounds (4%). Motor vehicle emissions are also a significant source of environmental exposure.

The substance is a gas, and therefore difficult to test by standard methods. No information on direct photolysis has been found, but the substance reacts rapidly in the atmosphere with hydroxyl radicals and other atmospheric oxidants. It has potential for the generation of low-level ozone and photochemical smog. No standard biodegradation tests are available, because of its high volatility. It is expected that the majority of any release will partition to the atmosphere. No measured bioconcentration factors (BCFs) are available, but low BCFs (13-19.1) have been estimated.

Few ecotoxicity data are available because of its high volatility. A 28-day NOEC for fish of 4.5 mg/l (*Brachydanio rerio, Pimephales promelas*) has been estimated using a quantitative structure-activity relationship (QSAR). No data are available for terrestrial organisms exposed via soil, but atmospheric exposure to a number of higher plants results in low toxicity. Following a detailed risk assessment in the European Union, this chemical is currently considered of low priority for further work for the environment.

1,3-Butadiene is absorbed via the lungs in animals and humans. There are no data for absorption via the oral or dermal routes of exposure, but since it is a gas it is reasonable to assume that uptake via these two routes would be minor compared with inhalation. The substance is widely distributed throughout the body. The first step in the metabolic pathway is the formation of epoxybutene. Further metabolism of epoxybutene to butenediol, diepoxybutane, and erythritol can occur. Excretion of 1,3-butadiene and its metabolites is mainly in the urine or in the breath.

This chemical is of low acute toxicity following single inhalation or oral exposure. The limited data available indicate it is of low acute toxicity to humans. The chemical does not exhibit skin irritation and there are no reports of skin or respiratory sensitisation.

Repeat-dose studies indicate the mouse to be more sensitive than the rat to 1,3-butadiene. Inhalatory repeated dose investigations in the rat produced minimal effects at 8000 ppm for 2 years. In the mouse, deaths primarily due to multi-organ tumour formation are observed at 20 ppm or above for a lifetime exposure. Additionally, in shorter-term studies in the mouse, the bone marrow has been identified as a target organ (1250 ppm).

1,3-Butadiene is genotoxic to bacterial cells *in vitro* (with metabolic activation). A number of *in vivo* studies demonstrate that it is mutagenic to somatic and germ cells in the mouse but not the rat. The metabolites epoxybutene and diepoxybutane are mutagenic in somatic cells in the mouse and/or hamster and in the germ cells of mice and rats. There is some evidence that 1,3-butadiene causes genetic damage in humans but the findings are inconsistent and overall the potential for human genotoxicity cannot be excluded.

The carcinogenicity of 1,3-butadiene has been studied in rats and mice, and there is a marked species difference in susceptibility. In the mouse, 1,3-butadiene is a multi-organ carcinogen. In the rat, the available study shows, even at high exposure concentrations, a lower tumour frequency and fewer tumour types mainly of a benign nature. The tumour types suggest hormonal influences may play a role in the rat carcinogenic response, and thus a non-genotoxic mechanism may underlie the tumour formation. It is considered that 1,3-butadiene has the potential to form genotoxic metabolites and therefore has the potential to be a genotoxic carcinogen in humans. A clear association between this chemical exposure and leukemia in humans has been demonstrated from one cohort-mortality study, with supporting evidence from a number of other studies. Thus, 1,3-butadiene may be carcinogenic in humans.

There are no adequate fertility studies available, although no evidence for an adverse effect on male fertility was seen in three dominant lethal assays in the mouse. The results of long-term toxicity and carcinogenicity studies indicate that the ovaries and testes are a target organ for 1,3-butadiene toxicity in mice (ovarian and testicular atrophy occurred at 625 and 1250 ppm in a 60-61 week repeated dose study, while malignant ovarian tumours developed in female mice exposed to 1,3-butadiene for up to 2 years). The testes are also a target organ in the rat (Leydig cell tumour formation was observed in a 2 year exposure study at 1000 and 8000 ppm). It is unclear what the effect on fertility would be from the changes that have been reported. The results of developmental studies in the rat and mouse suggest development effects are secondary to maternal toxicity and are of low concern for human health. There are no human data available for reproductive parameters.

Exposure to 1,3-butadiene is well controlled, there is only limited information regarding occupational exposure. Although this chemical is not added to consumer products, consumer exposure arises as a result of cigarette smoking (including passive smoking), and there may be exposure to residual monomer in products manufactured from synthetic polymers. Indirect exposure via the environment occurs mainly as a result of emissions from polymer production facilities.

NATURE OF FURTHER WORK RECOMMENDED

SIAM 4 agreed that the results of an ongoing epidemiology study might lead to a need for further action. Further information will be available to update the SIAR following completion of a risk assessment review within the European Union.