SIDS INITIAL ASSESSMENT PROFILE

CAS No.	590-86-3
Chemical Name	3-Methylbutanal (Isovaleraldehyde)
Structural Formula	CH_3-CH(CH_3)-CH_2-CHO

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Isovaleraldehyde is an irritating fluid of unpleasant odor, which at excessive doses may be absorbed into the body via all routes of exposure (oral, dermal and inhalation). Under practical conditions the irritation potential and chemical reactivity, however, would preclude significant systemic absorption. Biotransformation occurs through the usual oxidative pathway, mediated by aldehyde dehydrogenase to isovaleric acid, which may be incorporated into the intermediary metabolism. Furthermore, isovaleric acid and – transiently - also isovaleraldehyde may arise from isovaleric alcohol (3-methylbutanol). For that reason, toxicity data from this alcohol and also from isovaleric acid may help in the assessment of potential systemic effects of isovaleraldehyde (i.e. this part of toxicity which is not mediated by the protein-reactive aldehyde function).

Isovaleraldehyde is low in general acute toxicity after oral, dermal or inhalation exposure, is clearly irritating to the eyes and is strongly irritant to the skin under occlusive conditions. The material is not regarded as a potent sensitizer which is a common experience for aliphatic aldehydes with a single aldehyde function in the molecule supported by the negative animal data from the structural analogous aldehydes n-butyraldehyde, n-valeraldehyde and 2-methylbutanal. Studies with repeated exposure in animals (subchronic toxicity) do not exist with isovaleraldehyde. However, the relatively uniform toxicity profiles of aldehydes allow an estimation of these endpoints on the basis of data and results, which have been obtained during the investigation of other structurally related aldehydes, such as propionaldehyde, n-butyraldehyde and isobutyraldehyde. For systemic effects in the tested aldehydes the NOAEL for oral uptake is 300 mg/kg in rats, with effects on blood at > 600 mg/kg bw (n-butyraldehyde). For inhalation, the NOAELs with respect to systemic toxicity are $\geq$ 150 ppm. Effects observed were reduced food consumption in females rats at 750 ppm (propionaldehyde); no systemic effects were found up to the highest concentration of 2,000 ppm in rats (n-butyraldehyde). At 4,000 and 8,000 ppm body weight depression and mortality were observed in 13-week and 2-year studies in rats (isobutyraldehyde). In the metabolic precusor (3-methylbutanol-1) the only effects at the highest dose of 1,250 mg/kg (drinking water, rats) were blood effects. With respect to irritation, there is a clear dependency on molecule size, water solubility and Log Pow, indicating a NOAEL for isovaleraldehyde of > 51 ppm; butyraldehydes show a distinct lower irritating potential than propionaldehyde. The genotoxicity of isovaleraldehyde was investigated in-vitro with negative results in the Ames test and questionable results on SCE-rate in human lymphocytes. The substance did not show DNA-damaging activity in a Bacillus subtilis study (Rec-Assay). A mouse micronucleus test after intraperitoneal administration in doses up to 100 mg/kg body weight was clearly negative with respect to clastogenicity

and impairment of chromosome distribution in the course of mitosis. Thus, there is no concern with respect to genotoxicity. At present, there is no concern for carcinogenic effects of isovaleraldehyde. The experiments with isobutyraldehyde indicate a LOAEL for non-neoplastic effects of 500 ppm with weak local effects in female rats. Prenatal toxicity investigations have been carried out with propionaldehyde in rats and isobutyraldehyde in rats and 3-methylbutanol-1 in rats and rabbits. In these studies no prenatal defects and no high systemic toxicity was observed; hence, also isovaleric acid is not expected to exert prenatal toxicity. Isovaleric acid is, furthermore, also physiologically formed during the catabolism of leucine.

The NOAELs derived from the toxicological endpoints show no concern for the workplace, consumers and in relation to direct and indirect exposure from the environment.

Environment

3-Methylbutanal has a log Kow of 1.3, a water solubility of 20 g/l and a vapour pressure of 61 hPa. Based on the high vapour pressure of the substance isovaleraldehyde tends to pass from water to air. The compound does not tend to adsorb on sediment/soil or accumulate in biota. According to Mackay I the target compartment for this substance is the atmosphere.

It can be concluded that 3-methylbutanal is biologically readily degradable from a BOD5/COD ratio > 60 %.

Short-term tests with fish, daphnids and algae are available. For *Daphnia magna* EC50-values of 210 mg/l (24 h) and 177 mg/l (48 h) based on nominal concentrations were found. For *Scenedesmus subspicatus* a EC50 of 80 mg/l and a EC10 of 33 mg/l based on nominal concentrations was obtained in a 72h test. In a flow-through study with *Pimephales promelas* a 96h-LC50 of 3.25 mg/l was found based on measured concentrations. With an assessment factor of 1000 a $PNEC_{aqua}$ of 3.3 µg/l was derived.

Exposure

The production level of 3-methylbutanal (isovaleraldehyde) in Germany is in the range of 1000 - 5000 t/a. A certain amount is exported (no data about volumes). There is no information about import volumes. The chemical is used as an intermediate for pharmaceuticals, pesticides, solvents and softeners. Consumer exposure is not expected.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.