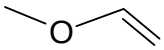
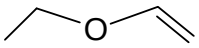
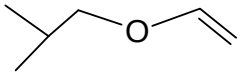
SIDS INITIAL ASSESSMENT PROFILE

Chemical category	Vinyl Ethers
Category Members: **CAS Registry Numbers and Chemical Names**	107-25-5 Methyl vinyl ether (MVE) 109-92-2 Ethyl vinyl ether (EVE) 109-53-5 Isobutyl vinyl ether (IBVE)
Category Members: **Structural Formulas**	107-25-5  109-92-2  109-53-5 

SUMMARY CONCLUSIONS OF THE SIAR

Category justification

The sponsored Vinyl Ether (VE) Category consists of short-chain (C3 to C6) vinyl ethers with a methyl (M), ethyl (E), or isobutyl (IB) group. The category members have similar structure and similar physico-chemical, environmental, and ecotoxicological properties, or follow a trend with respect to these properties. The toxicological profiles of all category members are very similar.

Human Health

Vapors of MVE, EVE and IBVE are rapidly absorbed after inhalation. All category members are aliphatic vinyl ethers and may undergo microsomal oxidation to unstable epoxides. IBVE hydrolyzes rapidly and completely to acetaldehyde and isobutanol in simulated gastric fluid. Much less hydrolysis occurs in simulated intestinal fluid or saliva.

The members of this category have a low order of acute toxicity. The acute inhalation LC_0-values (rat, 4 hrs) of MVE, EVE and IBVE were 47.9, 21.2 and 21.1 mg/l for MVE, EVE, and IBVE, respectively. There were no signs of toxicity noted in rats exposed to MVE; marked apathy and depressed breathing were seen during exposure to EVE. These signs subsided after the exposure ended and were absent on the next day. In humans, EVE has an anesthetic effect, and may cause salivation, nausea, vomiting, and circulatory and respiratory depression. Apathy, staggering and depressed breathing were noted in rats exposed to IBVE. No signs of toxicity were found in rabbits after 24 hours of occlusive treatment with 8.0 ml/kg bw of MVE, and no mortalities occurred after the same treatment with 15 080 mg EVE/kg bw or 15 380 mg IBVE/kg bw. The oral LD_{50} values in rats for EVE and IBVE were determined as 6153 mg/kg bw and > 7700 mg/kg bw, respectively. Signs of toxicity were only reported for IBVE and included dyspnea, staggering, and reddish encrusted eyes.

EVE was not irritating to the skin of rabbits. IBVE (of unknown purity) was a skin irritant in rabbits after 2 or 24 hours of occlusive treatment. Cold, liquid MVE, EVE and IBVE were all slightly irritating to the eyes of rabbits. There were no studies on the skin or respiratory sensitization potential of MVE, EVE or IBVE available.

Repeated dose toxicity studies were performed on rats by the respiratory route with MVE and IBVE. MVE was tested in 28-day studies according to OECD TG 412, and IBVE in a 90-day combined repeated toxicity and reproduction/developmental toxicity screening study according to OECD TG 422. No mortalities occurred in any of these studies at concentrations up to and including 60 mg/l MVE, and 8.3 mg/l IBVE. Exposure to high concentrations of MVE (12 - 60 mg/l) led to increased liver weights in male and female rats. Blood clotting times

were increased and total protein decreased in all male dose groups in the study using 1.2 – 60 mg/l, but this effect was not confirmed in a second study using 0.36 - 3.6 mg/l MVE. Following inhalation of 60 mg/l, atrophy in the region of the olfactory epithelium was observed on histological examination of the nasal mucosae. The NOAEL values were 8.4 mg/l MVE for female rats and 3.6 mg/l MVE for male rats. The main target organ of IBVE was the upper respiratory tract (hyperplasia of the respiratory epithelium, decrease of the secretory mucous cells, slight degeneration of the olfactory epithelium) at 2.08 or 4.16 mg/l IBVE. Based on these findings the NOAEL was 0.208 mg/l IBVE. Furthermore, changes in some blood parameters were seen in female animals at 2.08 mg/l. High serum triglyceride and cholesterol levels were noted in high-dose parental females; the effect was less pronounced in non-pregnant females and absent in males. Increased liver and kidney weight changes were noted in high-dose males and intermediate and high-dose non-pregnant females. There was no treatment-related effect in the neurofunctional tests (Functional Observation Battery and Motor Activity Test) at any dose level. The systemic toxicity of EVE after repeated inhalation is expected to be similar to that observed with MVE and IBVE.

MVE, EVE and IBVE were not mutagenic in the Ames test or in mammalian cell systems (EVE, IBVE) both in the absence and presence of metabolic activation. EVE and IBVE did not induce chromosomal aberrations in Chinese Hamster cells. *In vivo*, MVE did not induce micronuclei in bone marrow of mice, exposed to MVE vapors at concentrations as high as 60 mg/l. The members of this category appear to have no potential to induce gene mutations or chromosomal aberrations.

No carcinogenicity study is known to exist on any of the category chemicals.

There were no specific fertility studies available for MVE and EVE. Testes weights and testes histology as well as sperm parameters were not affected in a 28-day inhalation study on rats up to and including the highest tested dose of 60 mg/l MVE. In female rats exposed during gestation days 5 through 15, the pregnancy rate, gestational parameters including resorptions, pre- and postimplantation losses, percentages of live fetuses, and sex ratios were not affected at any dose level up to the highest tested dose of 47 mg/l MVE. Because of the short exposure periods in these studies, no firm conclusions can however be drawn with regard to the reproductive toxicity of MVE. The toxicity of IBVE to reproduction was tested according to OECD TG 422 in a rat inhalation study with an extended exposure period of 90 days for parental animals at 50, 500, and 2000 ppm (i.e. 0.208, 2.08, and 8.3 mg/l). Reproduction parameters (male and female fertility indices, gestation index, and duration of gestation) and histology of male and female reproductive organs were not affected at any dose. Therefore, the NOAEL for reproduction toxicity was 2000 ppm IBVE for male and female rats, i.e. 8.3 mg/l. There is no data to suggest that members of this category will represent a hazard for fertility.

In a developmental toxicity study performed with MVE according to OECD TG 414, slight systemic toxicity (decreased corrected terminal body weight) was noted in all dams treated with 5000, 10 000, or 19 500 ppm (12, 24 or 47 mg/l). No malformations were noted in the offspring, but there was an increase in the incidence of skeletal variations (delayed ossification of neck, tail, paws and sternebra at 10 000 and 19 500 ppm). The developmental NOAEL was at 5000 ppm, i.e. 12 mg/l; the LOAEL for maternal toxicity was also at 5000 ppm (12 mg/l).

As noted above, a systemic NOAEL of 0.208 mg/l was derived for IBVE in the 90-day inhalation study on rats according to OECD TG 422. In the progeny, no other effect than a slightly, yet significantly reduced live born index (93 versus 100 % in controls) was noted at the highest tested dose of 2000 ppm (8.3 mg/l). Therefore, the developmental NOAEL was 500 ppm (2.08 mg/l). No reproduction and developmental toxicity data exist for EVE. Based on the structural similarities between the members of this category and the similarity of their toxicity profiles, data for the tested vinyl ethers are considered to be predictive for EVE, i.e. it is expected, that there will be no developmental toxicity in the absence of maternal toxicity.

Environment

The three members of the category, MVE, EVE, and IBVE, are colorless liquids. Above the boiling point (5.7 °C) MVE is a colorless gas. The boiling points for EVE and IBVE are 36 and 83 °C, respectively. The densities at 20 °C are 0.747 g/cm^3 (MVE, liquefied gas), 0.754 g/cm^3 (EVE) and 0.769 g/cm^3 (IBVE). The substances are volatile with vapor pressures from ca. 90 hPa (IBVE) to ca. 1700 hPa (MVE) at 20 °C. The category members are soluble in water (0.7 – 17.1 g/l at 25 °C) and the Henry's Law constants of 264 – 680 Pa*m³/mol at 20 °C indicates high potential for volatilization. The log K_{OW} values of 0.4 (MVE, calculated), 1.6 (EVE, 25 °C, measured), and 3.1 (IBVE, 25 °C, measured) and the calculated BCF values of 1.3 – 81 (IBVE) show a low to moderate potential for bioaccumulation.

According to Mackay Level I, the category members would distribute to a great extent to air (98.7 – 99.6 %). On Mackay, Level III shared emissions (scenario 4) to air (60 %), water (30 %), and soil (10 %) would lead to a

predominant distribution into water for all category members, whereas in the other scenarios (1-3), the category members would remain in the compartment they were released into. In the atmosphere, the category members will rapidly be photodegraded by reactions with OH radicals (calculated half-lives ($t_{1/2}$) for a 24-h day: 8 – 11 hours).

Calculated half-lives for hydrolysis of EVE and IBVE at pH 7 are 42 d and 35 d respectively, and at pH 5 these are 10.0 h and 8.4 h, respectively.

As shown in ready (sealed system) and inherent biodegradability (unsealed system) tests, IBVE is biodegradable: 63 % biodegradation after 28 days in a OECD TG 310 test but failing the 10-days window, and 70 % BOD of COD after 5 days in a BOD_5 test following the German Industrial Standard DIN 38409, part 51. In a similar test, EVE was not biodegraded: 10 % BOD of COD after 5 days. However, the members of the category will also be easily eliminated from water by volatilization (EVE: 100 % elimination by volatilization after 5 days in an OECD TG 302B test). Experimental data are not available for MVE.

Acute aquatic toxicity studies in sealed test systems are available for IBVE. The results for fish (*Danio rerio*; LC_{50} (96 hours): 28.3 mg/l), invertebrates (*Daphnia magna*; EC_{50} (48 hours): 46.3 mg/l), and algae (*Desmodesmus subspicatus*; 72 h E_bC_{50} = 32.2 mg/l; 72 h E_rC_{50} = 45.9 mg/l) indicate moderate toxicity to aquatic life. The acute toxicity result for EVE on *Daphnia magna* (closed system; 48 hour EC_{50}: > 100 mg/l) showed that EVE is of less ecotoxicity than IBVE. The assumed trend in aquatic toxicity from MVE over EVE to IBVE was confirmed by QSAR predictions on aquatic toxicity. Concerning toxicity to microorganisms, only data from studies with unsealed test systems are available. According to the EU risk assessment procedure (EC, 2003) a $PNEC_{aqua}$ of 0.028 mg/l was obtained by applying an assessment factor of 1000 on the lowest effect concentration, the result of the acute *Danio rerio* test with IBVE.

Exposure

The industrial method used for the production of vinyl ethers in the Sponsor country is the reaction of acetylene with the corresponding alcohols in the presence of potassium hydroxide in the liquid phase under pressure and temperatures between 150 and 180 °C (Reppe vinylation). Because of the applied reaction conditions and the handling of gaseous compounds the manufacturing facilities are designed as closed systems. In the Sponsor Country, the vinyl ethers of this category are manufactured at one single site and processed in plants at the same location.

The annual world production capacity in 2004 for the members of the vinyl ethers category (MVE, EVE, IBVE) was estimated at 40 000 – 80 000 tons, subdivided into 10 000 – 20 000 tons/a for Europe, 10 000 – 20 000 tons/a for NAFTA (USA), and 20 000 – 40 000 tons/a for Asia/Pacific.

MVE is used as a starting material for polymers/copolymers (coatings, adhesives), leather processing agents, biocides, construction material, and personal care products. EVE is a starting material for polymers/copolymers (coatings, adhesives), flavors, and pharmaceuticals. IBVE is mainly used as starting material for copolymers (e.g. in coatings for food packaging materials, adhesives), pharmaceuticals, and dyes (fuel markers).

During manufacture and processing of vinyl ethers, worker exposure is controlled by the use of closed systems, industrial hygiene controls, and personal protective equipment. In the Sponsor country, any risk of accumulation of vinyl ethers or its impurities is minimized by natural ventilation, as the chemical is produced in closed systems installed in open air. At processing sites, the exposure of workers is minimized by vapor abstraction. Prior to repair and maintenance work, vessels, pipes and other equipment is rinsed to remove any residual vinyl ethers. In the Sponsor country, the main part of the production volume is processed internally and transferred via pipelines to other plants at the same site. Only small amounts are bottled in trading units in an air-conditioned room using an exhaust device. Dedicated systems designed to handle vinyl ethers are typically used for loading and unloading purposes, and spill prevention procedures are in place. Drum filling stations are fully encapsulated and vapor abstraction is in place to prevent the formation of explosive atmospheres and to minimize exposure. The vent gases are either incinerated or cleaned by means of a scrubber.

At the production and processing sites, workers wear personal protective equipment which includes gloves, face shields and safety goggles in view of the low pH during processing. During repair and maintenance operations, and during drum emptying operations, respiratory protective equipment is additionally used. Exposure to vinyl ethers via air is routinely controlled by personal air sampling.

Consumer exposure to residual MVE, EVE or IBVE may occur through the use of products made from vinyl ether polymers or copolymers. However, this exposure is considered to be very low, since most of the marketed vinyl ether polymers and co-polymers are heat-treated and potentially existing residual vinyl ethers are expected to evaporate during this process. In the EU, the use of IBVE in food packaging materials is restricted to a

maximum of 5 mg/kg in the finished article, because of limited data which did not allow establishing an acceptable daily intake.

Releases into the environment may occur during manufacturing and processing in the industry. According to the data reported to the German Emission Register, during production and internal processing at BASF AG, Ludwigshafen, 127 kg/a of MVE, less than 100 kg/a of EVE, and 3903 kg/a of IBVE were emitted to air in 2004. The mean measured IBVE concentrations in the effluent of the industrial wastewater treatment plant (wwtp) of BASF AG were below the limit of detection (20 µg/l) in 2004. Neither MVE nor EVE was monitored in the effluent of the WWTP at this production and processing site.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemicals of this category are currently of low priority for further work. The chemicals possess properties indicating a hazard for human health (irritation, repeated-dose toxicity by high dose treatment, all category chemicals may produce explosive atmospheres with air, the lower explosive limits are in the range between 0.7 and 2.2 vol.%). Exposure in occupational settings is controlled, and consumer exposure is anticipated to be low. Countries may wish to investigate any exposure scenarios that have not been presented by the Sponsor country.

Environment: The chemicals of this category are currently of low priority for further work. The chemicals possess properties indicating a hazard for the environment (acute toxicity to fish, aquatic invertebrates and algae: LC/EC_{50} between 10 and 100 mg/l). However, the chemicals are of low priority for further work for the environment because of their volatility, their fast photodegradation and limited potential for bioaccumulation.