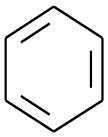
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	**71-43-2**
Chemical Name	**Benzene**
Structural formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The toxicokinetics of benzene have been studied in both animals and humans. The key findings suggest that benzene is absorbed by all routes (inhalation, dermal and oral) with inhalation as the most important route of exposure. Benzene is rapidly distributed in the body and higher concentrations are found in fat and in lipid rich tissues compared to blood. After absorption via inhalation, the dermal or the oral route, most of benzene is metabolized and the metabolites are excreted after phase-II-conjugation mainly in the urine. Oxidative metabolism of benzene is a prerequisite to toxicity and follows similar pathways in humans and animals. The liver is the major site of benzene metabolism, but metabolism in the bone marrow may be associated with the haematotoxic and leukaemogenic effects of benzene.

There is considerable support for the idea that benzene works via a multiple metabolite type of mechanism, that not just one metabolite is responsible for benzene toxicity but multiple metabolites are involved. These multiple metabolites of benzene are capable of interacting to induce cytotoxic and cytogenetic responses particularly in bone marrow myeloid and stromal cells. There are apparent species differences in the rate of benzene metabolism, in Vmax at higher exposure to benzene, and in the proportion of toxification (oxidative) versus detoxification (conjugation) metabolic pathways.

Acute oral toxicity for rats ranges from 810 mg/kg bw to 10000 mg/kg bw. Experiments using high numbers of rats suggest that the oral LD50 is above 2000 mg/kg bw. Depending on the dose the main clinical signs are sedation and narcosis. Pathological findings include among others hyperaemic and haemorrhagic lungs, adrenals and spine. Acute inhalation toxicity is low with a LC50 value of 44500 mg/m^3 after a 4-hour exposure to female rats (OECD TG 403). Depression of the central nervous system appeared to be related to death. The main pathological findings were congestion of the lungs and liver. A dermal LD50 value of >8260 mg/kg bw for rabbits and guinea pigs has been reported.

An oral uptake of about 15 ml benzene by humans (176 mg/kg bw) can cause collapse, bronchitis and pneumonia. The direct aspiration of liquid benzene into the lungs causes immediate pulmonary oedema and haemorrhage at the site of contact with the pulmonary tissue. Very high concentrations of benzene vapours produce narcotic effects and can lead to death by respiratory arrest. Fatal effects can occur after inhaling a benzene concentration of 65000 mg/m^3 for 5-10 minutes. Exposure of 30 minutes to benzene concentrations of 25000 mg/m^3 can be dangerous to life threatening. After inhalation exposure to 160-480 mg/m^3 for 6 hours headache and lassitude occur while after inhalation of 80 mg/m^3 for 6 hours no acute toxic effects were documented. The odor threshold is reported to be 4.8 mg/m³. In a report on three fatalities of acute benzene poisoning by acute dermal and inhalation exposure second degree chemical burns to face, trunk and limbs, haemorrhagic lungs and pulmonary oedema were documented. A relationship between chemical burns and death was not mentioned.

In a Draize test with rabbits according to OECD TG 404 benzene is irritant to the skin. Undiluted benzene caused serious damage to eyes. Inflammation and slight swelling of the eyelids, and questionable or just perceptible transient superficial necrosis of the cornea involving an area of less than 50% were documented. Airborne concentrations up to 972 mg/m^3, as used in different inhalation studies, did not reveal local effects in the respiratory tract of mice. In humans, high concentrations of benzene vapour are irritant to mucous membranes of the eyes, nose and respiratory tract. Second

degree chemical burns of the face, trunk and limbs after acute benzene vapour poisoning are reported.

Data on animal tests on sensitization is not available. Furthermore no reports are available on skin sensitization or respiratory hypersensitivity for workers . That is expected taking into account the chemical structure of benzene..

Repeated inhalation exposure in mice using different exposure regimes was effective at concentrations from 32 mg/m^3 benzene (LOAEC). No NOAEC could be derived.

The interaction of inhaled benzene with hematopoietic stem cells (multipotential hematopoietic stem cell CFU-S, granulocyte/macrophage progenitor cell CFU-GM), marrow and spleen cells was studied in three experiments using different exposure regimens and concentrations. Exposure of male CD-1 mice for 6 hr/d for 5 days to 3.5, 32, 320, 979, 1930, 4083, 7731, or 15558 mg/m³ showed that spleen weight, femoral and splenic cellularities (total number of nucleated cells, granulocytes, lymphocytes and nucleated red cells), total number of CFU-S in femur and spleen, and the number and concentration of splenic CFU-GM were significantly reduced at concentrations ≥ 320 mg/m³. In femur, absolute numbers of CFU-GM were marginally reduced at ≥ 320 mg/m³ and significantly at all higher doses, whereas the fraction of CFU-GM was increased to variable amount in most doses of ≥ 320 mg/m³ and higher. Exposure to 979 mg/m³ resulted in reduced concentration of splenic and marrow CFU-S. In peripheral blood, WBC, neutrophils and lymphoctes were depressed ≥ 320 mg/m³. RBC counts were depressed only at the two highest exposure levels.

A further experiment with exposure of CD-1 mice to 32 mg/m³ over 50 days (6 hr/d, 5 d/w) resulted in higher spleen weight, elevated splenic cellularity and increased number and concentration of CFU-S, but no changes in the CFU-S content of bone marrow were detected. CFU-GM were not evaluated in this experiment. No differences in the peripheral blood, bone marrow, or body weight were detected in exposed mice.

Exposure of CD-1 mice to 966 mg/m³ (6 hr/d, 5 d/w) for 26 weeks showed lower spleen weight, marked depression in marrow and spleen cellularity with depressed marrow and spleen CFU-S (total number and concentration) and marrow CFU-GM (total number and concentration) and spleen CFU-GM (total number). Marked changes in the peripheral blood included depressed WBC counts, RBC counts and percentages of lymphocytes, while the number of neutrophiles appeared to be elevated.

In vivo and in vitro evaluations of hematopoiesis, specifically erythropoiesis, were performed with C57B1/6J male mice by exposure of 32 mg/m³ benzene (6 hr/d, 5 d/w) for up to 178 days. The numbers of circulating RBC and lymphocytes were significantly depressed in benzene-exposed mice. At 178 days, the exposed mice exhibited depressions in splenic nucleated cellularity and in splenic nucleated RBC numbers. Bone marrow cellularity and marrow-nucleated RBC counts were unaffected by the exposures. Benzene exposed mice showed a progressive decline in bone marrow and splenic colony-forming unit-erythroid (CFU-E) colonies during the exposure period, reaching 5% and 10%, respectively, of control values after 178 days.

Short-term inhalation exposure to 32, 99, 320, and 960 mg/m³ benzene vapour to male C57B1/6J mice on 6 days (6 hr/d) produced a depression of lymphocyte counts at all dose levels and at ≥ 320 mg/m³. Reduced numbers of B-lymphocytes in the femural bone marrow and reduced T-lymphocytes in the spleen were also observed at ≥ 320 mg/m³.

In Sprague-Dawley rats exposure to benzene concentrations of 3.2, 32, 96 or 960 mg/m³ (6 hr/d, 5 d/w, whole body exposure) for up to 13 weeks (method similar to OECD TG 413) showed a decrease in WBC counts and percentage of lymphocytes at 960 mg/m³. The NOAEC for hematological effects on peripheral blood circulation is 96 mg/m³.

In NTP studies, B6C3F1 mice were evaluated for cumulative toxicity of benzene in 17 week and two-year studies. In the 17-week studies, mice of each sex were administered 0, 25, 50, 100, 200, 400 or 600 mg/kg bw/d benzene in corn oil by gavage. Mice receiving 100 mg/kg bw or higher showed lower final body weights. Dose-related leucopenia and lymphocytopenia were registered in male mice at ≥ 50 mg/kg bw and in female mice at ≥ 400 mg/kg bw. In the NTP cancer study, mice of each sex were administered to 0, 25, 50, or 100 mg/kg bw benzene by gavage (5 d/w) for 103 weeks. Weight gain reductions occurred in high dose males and females. Hematologic effects were limited to lymphocytopenia and associated leukocytopenia at all doses. Thus, the LOAEL in chronic oral studies

on mice was 25 mg/kg bw/d.

In a NTP study Fischer 344 rats were evaluated for cumulative toxicity of benzene in 17-week studies and two-year studies. In the 17-week study, rats were administered 0, 25, 50, 100, 200, 400 or 600 mg/kg benzene in corn oil by gavage. Final body weight was depressed in both sexes at doses of ≥ 200 mg/kg bw. Dose-related leucopenia and lymphocytopenia were observed in male rats at ≥ 200 mg/kg bw and in female rats at ≥ 25 mg/kg bw. In the spleen, lymphoid depletion of B-cells was evident in both sexes at ≥ 200 mg/kg, and increased extramedullary hematopoiesis was seen in male and female rats at 600 mg/kg bw/d. In the NTP cancer study male rats were administered to 0, 50, 100, or 200 mg/kg bw and female rats to 0, 25, 50, or 100 mg/kg bw benzene by gavage, 5 d/w for 103 weeks. Weight gain reductions occurred in mid and high dose males rats, and high dose female rats. Hematologic effects were limited to lymphocytopenia and associated leukocytopenia in all male rat groups; a similar but less pronounced response was observed in females during the same time period. Histopathology revealed increased incidences at all dose groups of lymphoid depletion in the spleen (male and female rats) and the thymus (male rats). The LOAEL in chromic oral studies on rats was 25 mg/kg bw/d for females and 50 mg/kg bw/d for males.

Besides of leukocytopenia and other effects on the lymphocyte cellularity several studies on the immune response revealed that benzene is suppressive on the cellular and humoral immunity of C57B1/6J mice at concentrations of 32 mg/m^3 and higher (6 hr/d, 6 d, inhalation) or of CD-1 mice at doses of 40 and 180 mg/kg bw/d, given orally via drinking water for 4 weeks.

Related to the benzene effects on the bone marrow and peripheral blood the mouse seemed to be more sensitive than the rat. Several studies showed that benzene exposure resulted in disparate toxic responses among various strains of mice.

Chronic benzene exposure in humans leads to depression of white and red blood cells. This effect is reversible after long time exposures (years) with low concentrations (reported concentration range: > 32-64 mg/m³). Exposure to 192 mg/m³ of benzene for about one week may be associated with an increased proportion of large granular lymphocytes, and not severe narrow effects nor specific cytopenias. At higher concentrations, benzene may lead to aplastic anaemia which can be fatal. A review suggests a fatal outcome in 13% of the cases (as opposed to 85% for idiopathic aplastic anaemia).

The prevalence of leucopenia correlates with the exposure concentration of benzene. Drawn from these data, the LOAEC for leucopenia is in the range between 40 mg/m³ and 64 mg/m³. A higher prevalence for leucopenia is given at concentrations above 320 mg/m³. The LOAEC for red blood depression may be somewhat lower at 32 mg/m³. Thus, for blood cell depression an overall LOAEC is suggested to be 32 mg/m³.

Recent case control studies showed that the most sensitive reaction in humans to chronic benzene exposure is lymphopenia. A collective of workers exposed to benzene concentrations in a range between 3.2 mg/m^3 and 100 mg/m^3 had significantly reduced lymphocyte counts as compared to a cohort of non-exposed workers. A NOAEC for that effect of 3.2 mg/m³ is derived from these studies.

Benzene did not induce in vitro gene mutations in bacteria using standard Ames test conditions (OECD TG 471). Weakly positive effects were obtained when, in presence of S-9 mix, S. typhimurium strain TA 1535 was incubated with benzene in a desiccator to enhance exposure. Mammalian cell gene mutation tests carried out in various human, mouse and Chinese hamster cells according to OECD TG 476 resulted in mixed results. Treatment of human lymphocytes and various animal cells in vitro with benzene can lead to chromosomal aberrations and SCEs (OECD TG 473, OECD TG 479). However, mixed results have been obtained. Negative findings may be due to insufficient activities of benzene-activating enzymes.

Benzene is an in vivo mutagen in mammals, especially chromosomal aberrations and micronuclei are induced. After oral application the lowest dose with observed mutagenic effect was about 25 mg/kg bw for acute as well as for long-term exposure (micronucleus tests in mice according to OECD TG 474). According to one report a single low dose of 3.2 mg/m³ induced micronuclei in bone marrow cells of rats after inhalation exposure (OECD TG 474). However, in investigations on chromosomal aberrations in rats according OECD TG 475 positive effects were obtained only at concentrations of 320 mg/m³ and higher (single exposure) or 32 mg/m³ and higher (repeated exposure). In mice, the lowest effective concentration is reported to be 32 mg/m³ (micronuclei after single exposure).

Studies with intraperitoneal administration on mice showed that benzene has the potential for induction of transplacental genetic effects. Only few valid data on germ cell mutagenicity in mammals are available. In mice chromosomal aberrations are induced in spermatogonia by oral doses ranging from 220 to 880 mg/kg bw (OECD TG 483).

Concerning human data it is reported that benzene exposure induces genotoxic effects in human lymphocytes in vivo. A fully reliable conclusion, however, cannot be drawn due to poor exposure data and methodological insufficiencies. Therefore, it is not possible to deduce a dose-effect relationship. It is unlikely that exposure levels up to 64 mg/m³ induce observable genotoxic effects in humans.

Benzene induced neoplasms in both sexes of different strains of mice and rats on multiple sites by inhalation and oral administration. Target organs of benzene induced carcinogenic effects in animals included the haematopoietic system and a spectrum of tissues of epithelial origin indicating that benzene is a multipotential animal carcinogen. Lymphomas were induced in several mouse studies, however not all studies demonstrated clearly increased lymphatic tumour rates. Additionally, the tumour responses were not homogeneous in different mouse strains.

Inhalation exposure of male C57Bl/6J mice for about 70 weeks to 960 mg/m³ benzene (6 hr/d, 5 d/w) resulted in the development of malignant lymphomas. However, benzene exposure of male AKR/J mice to 320 mg/m³ for lifetime did not induce significantly lymphomas. In mice of each strain, exposure to benzene produced anemia and lymphocytopenia, but only in the 40 male C57Bl/6J mice neutrophilia, granulopoietic or myeloic bone marrow hyperplasia and in six males lymphocytic lymphoma with thymic involvement, one plasmacytoma, and one hemocytoblastic leukaemia was reported.

In the oral NTP study increased incidences of malignant lymphomas were reported in B6C3F1 mice given doses of 25, 50, or 100 mg/kg bw/d benzene in corn oil (5 d/w) for 103 weeks. Bone marrow hematopoietic hyperplasia was observed at increased incidences in dosed mice of each sex. The incidences of Zymbal gland carcinomas in mid and high dose male mice and in high dose female mice were greater than in controls. In the same dose groups, the incidences of epithelial hyperplasia of the Zymbal gland were also increased. Incidences of squamous cell papillomas or carcinomas (combined), hyperkeratosis, and epithelial hyperplasia of the forestomach were increased in some dosed groups of male and female mice.

Only few data existed which described the induction of myelogenous leukaemias. An increased rate of leukaemias without specification of the predominant cell type was found in RF/J mice treated with 500 mg/kg bw/d for 52 weeks.

No clear effect on the extent of lymphoma formation was observed in long term inhalation studies on pregnant Sprague-Dawley rats (13 week-old adults) with exposure from the twelfth day of pregnancy on to 650 mg/m³ for 7 weeks (4 hr/d, 5 d/w), then on 12 weeks to 640 mg/m³ for 7 hr/d, followed by 980 mg/m³ (7 hr/d, 5 d/w) for 85 weeks. The 12-day old offsprings were exposed to a similar treatment schedule; treatment was stopped after 104 weeks. Leucopenia mainly due to lymphocytopenia was evident in male and female offsprings following 104 weeks of exposure. At 150 weeks after study begin, benzene caused in animals treated for 104 weeks increased incidences of carcinomas of Zymbal gland, oral cavity, nasal cavity, skin, and forestomach and hepatomas.

Oral treatment of Fischer 344 rats for 2 years (NTP studies) with 50, 100, or 200 mg/kg bw/d (males) and 25, 50, or 100 mg/kg bw/d (females) increased the incidences of Zymbal gland carcinomas in mid and high dose male rats and in all females. Benzene was associated with increased incidences of neoplasms of the skin and oral cavity of rats. The incidences of squamous cell papillomas and squamous cell carcinomas of the skin in the high dose male rats were greater than in controls. Increased incidences of uncommon squamous cell papillomas or squamous cell carcinomas (combined) of the oral cavity were observed in dosed male and female rats. However, no increased incidence of tumours of the lymphatic system were observed in Fischer 344 rats, and no incidences in lymphomas were observed in Sprague-Dawley and Wistar rats (poorly documented, Maltoni, 1989).

Increased frequencies of leukaemia in comparison to controls were found in benzene exposed Sprague-Dawley rats and Wistar rats given orally 50 or 250 mg/kg bw/d for 52 weeks and 500 mg/kg bw/d for 104 weeks.

There is sufficient scientific evidence from the numerous human epidemiological studies to assume a causal relationship between benzene exposure and acute non-lymphatic leukaemia. It is unclear,

however, if there exists a threshold level of benzene exposure above which the risk of leukaemia significantly increases. Previous studies concluded that the leukaemic risk is increased at relatively low levels of benzene exposure. Using modeling techniques, which were based on revised estimates of the benzene exposures in the Pliofilm cohort with an update of the follow-up (until 1987) analyses assume a negligibly increased mortality attributable to benzene if the average exposure is < 3.2 mg/m³ over 40 years. From the recently published cohort study from exposed Chinese workers an elevated risk was shown for acute non-lymphotiac leukaemia and myelodysplastic syndrom at average benzene exposure levels of less than 32 mg/m³.

The data of the meta-analysis by Wong and Rabe (1995) have been used to define a NOAEC in misinterpreting the results as an indication that a benzene exposure related carcinogenic effect can be excluded at the mean exposure level (700 µg/m³) of the 19 different studies. However, the data do not allow to establish such a threshold level with the appropriate certainty.

The issue of linearity in the dose-response relation of benzene induced haematotoxicity and leukaemia was addressed by various publications. Especially for extrapolation to low doses, arguments have been presented for a non-linear, a sub-linear, and a supra-linear dose relationship. In addition, arguments have been presented for epigenetic factors responsible for leukaemia induction which lead to the suggestion of a threshold approach. Nevertheless, present knowledge is insufficient to support any quantitative deviation from the linear dose-response curve, at least from a regulatory point of view . Recent data support the view that the risk of developing acute myeloic leukaemia and chronic lymphocytic leukaemia (but not non-Hodgkins lymphoma or multiple myeloma) is increased at very low benzene exposure without clear cut-off concentration.

Inhalation studies with Sprague-Dawley rats (32, 160, and 1600 mg/m^3, day 6 to day 15 of gestation, 7 hr/d) showed that benzene may lead to fetal growth retardation as evidenced by decreased fetal body weight and body length, and/or skeletal variation including delayed ossification at 160 mg/m³ and higher. A NOAEC developmental toxicity (no fetal growth retardation) of 32 mg/m³ has been derived from this study on rats. The NOAEC maternal toxicity was 32 mg/m^3. No specific embryotoxic and teratogenic potential could be revealed in further teratogenicity and developmental toxicity studies with rats, mice and rabbits. An available non-guideline fertility study in Sprague-Dawley rats is recognised from which it appears that female fertility is not affected at inhalation exposures (6 hr/d, 5 d/w) of up to and including 960 mg/m^3, however, this study is not considered sufficient and adequate for overall assessment of an impairment of male/female fertility. Data from 90 day inhalation repeated dose toxicity studies (3.2, 32, 96 and 960 mg/m^3, 6 hr/d, 5 d/w) revealed some effects of benzene to the organs of the reproductive system in CD-1 mice (histomorphologic changes and decrease in mean testes weights) at 960 mg/m^3 (NOAEC 96 mg/m³), but not in Sprague-Dawley rats. The significance of this finding in relation to possible impairment of fertility remains unclear, since adequate functional studies are not available. Since benzene is a germ cell mutagen and genotoxic carcinogen the substance has the potential to be toxic to reproduction. Therefore, further testing is not warranted.

Evidence from human data for an effect of benzene exposure on female reproduction is not sufficient to demonstrate a causal association due to poorly designed studies and inadequately quantified exposure to benzene as well as to other chemicals. Epidemiological studies in males on effects on fertility are not available. Likewise epidemiological studies implicating benzene as a developmental toxicant have many limitations thus not providing sufficient information to assess the effects on the human fetus.

Environment

Benzene is a clear colourless liquid with a melting point of 5.5°C and a boiling point of 80.1°C (at 1013 hPa). Benzene has a log Kow of 2.13, a water solubility of 1.8 g/l (at 25°C)and a vapour pressure of 99.7 hPa (at 20°C). With a Henry's law constant of 432 Pa m^3 mol^{-1} benzene is rapidly volatilized from aqueous solution and surfaces.

Benzene does not undergo hydrolysis or direct photolysis. It is classified as readily biodegradable in sewage treatment plants, the hydrosphere, sediments and soils. In the atmosphere benzene will be degraded by reaction with OH radicals with a half-life of 13.4 days.

Level III calculations show that benzene has the tendency to stay airborne, when released to air and to volatilise with a half-life of 11.5 d from water to air, when released into surface waters. According to this model the favourite target compartment of benzene is air with 99,0%, followed by water with 0.9%.

Bioaccumulation studies with fish show that benzene has a low bioaccumulation potential. BCFs

related to whole fish of 11 and < 10 were found.

For benzene short- and long-term studies with fish, daphnids and algae are available. Fish were the most sensitive species in both short- and long-term tests. The following results were found in long-term tests: Pimephales promelas (FELS): 32d-NOEC = 0.8 mg/l; Ceriodaphnia dubia: 7d-NOEC = 3 mg/l; Selenastrum capricornutum: 72h-EbC50 = 28 mg/l, 72h-EbC10 = 8.3 mg/l. All effect values are related to measured concentrations. With an assessment factor of 10 a PNEC of 0.08 mg/l was derived from the fish early-life-stage study.

The following results were found in short-term tests: Oncorhynchus mykiss: 96h-LC_{50}=5,3 mg/l; Daphnia magna: 48h-EC_{50}=10 mg/l;

Benzene seems not to be of concern for plants with regard to exposure via the atmosphere except at very high concentrations. No formal PNEC was established because of lack of appropriate long-term studies.

Exposure

In the European Union, 7,084 kt/a of pure benzene are produced and isolated as chemical intermediate. The worldwide production volume in 1995 was 22,300 kt. The most important secondary products manufactured from benzene in Western Europe in 1994 were ethylbenzene (52 %), cumene (20 %), cyclohexane (13 %), nitrobenzene (9 %), alkylbenzene (3 %), maleic anhydride (2 %) and chlorbenzene (1 %). Small quantities are also used as a laboratory reagent and solvent. Petroleum refinery streams containing benzene are blended with other petroleum streams to formulate petrol. This benzene used in petrol is in addition to the benzene of chemical intermediate production.

Benzene is released from a number of man-made sources. The primary sources of environmental benzene are automobile exhaust emissions, evaporative losses and refuelling emissions. Benzene in automotive exhaust is a mixture of incompletely burned benzene and benzene produced in the motor during combustion through dealkylation of toluene and xylenes. From industrial sources, it primarily enters the environment as fugitive emissions from industrial intermediate production and processing operations and through air emissions from waste water treatment plants.

Natural sources of benzene emissions such as vulcanos and forest fires exist.

Benzene is used and emitted in large quantities. Because benzene is a volatile organic compound, it is mainly emitted to the air and emissions to soil and water partly lead to emission to the air. As a result most of the benzene is found in the air compartment.

Exposure of consumers to benzene may result from filling gasoline at filling stations and from use of contaminated paints and due to release from car interior accessories when driving a car. Inhalation is the dominant pathway for benzene exposure in humans, whereas oral and dermal exposure can be neglected. The following exposure estimates of benzene concentrations for consumers are available: filling gasoline (1.3 mg/m^3), painting (0.017 mg/m^3), and from car interior accessories 0.012 (1.3 mg/m^3).

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

Human Health:

The chemical is a candidate for further work.

The chemical pocesses properties (repeated dose toxicity, mutagenicity, carcinogenicity, suspicion in reproductive toxicity) indicating a hazard to human health. Due to the widespread use of the substance leading to continuous exposure member countries are invited to perform an exposure assessment, and if necessary, a risk assessment for human health.

Note: A risk assessment to be performed in the context of the EU Existing Substances Regulation (793/93/EEC) in the European Union reveals concern for consumers due to mutagenic and carcinogenic properties of the substance.

Benzene exposure arising from handling gasoline is not formally a part of the EU risk assessment.

Regarding the very low benzene exposure from materials in new cars (interior accessories) further measurements are needed.

Occupational risk assessment revealed concern for all exposure scenarios at the workplace (risk reduction measures concerning benzene in gasoline should await a special risk assessment of gasoline).

Benzene will be easily absorbed after inhalation and skin contact. Mainly inhalation is the cause for relevant exposure levels. Internal body burdens after dermal exposure generally are low because of rapid evaporation of benzene. If, however, skin contact is prolonged either by inappropriate use of gloves or by repeated initial contacts, dermal exposure might become relevant concerning health risks at the workplace

From the toxicological point of view areas of concern are mutagenicity, carcinogenicity, repeated dose toxicity and reproductive toxicity. Several working scenarios give rise to concern under different aspects. In case of inhalative exposure levels below 1 ppm (3.2 mg/m³) or prolonged skin contact concern concentrates on the aspects of mutagenicity and carcinogenicity. In the light of these two endpoints it should be reflected whether the occupational exposure limit of 1 ppm, recently adapted in the EU, is considered to be sufficient to reduce the occupational risks. Furthermore measures to prevent prolonged skin contact appear indicated.

Environment:

The chemical is a candidate for further work. The chemical possesses properties indicating a hazard for the environment (aquatic toxicity). Although the chemical is readily biodegradable and has a low potential for bioaccumulation, concern was identified in a risk assessment performed in the context of the EU Existing Substances Regulation (793/93/ECC) for industrial waste-water treatment plants and surface water receiving effluents from production sites. Other member countries are invited to perform an exposure assessment, and if necessary a risk assessment for the environment.