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Benzene in Drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

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Preface

One of the primary goals of WHO and its member states is that "all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water." A major WHO function to achieve such goals is the responsibility "to propose regulations, and to make recommendations with respect to international health matters ...."

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as International Standards for Drinking-Water. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO Guidelines for drinking-water quality (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A "final task force" meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health

Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues, and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.

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GENERAL DESCRIPTION

Identity

CAS no.: 71-43-2
Molecular formula: C_6H_6

Physicochemical properties (*1,2*) [Conversion factor in air: 1 ppm = 3.2 mg/m^3 at 20 °C and 101.3 kPa]

Property	*Value*
Physical state	Colourless liquid
Melting point	5.5 °C
Boiling point	80.1 °C
Density	0.88 g/cm^3 at 20 °C
Vapour pressure	13.3 kPa at 26.1 °C
Water solubility	1.8 g/litre at 25 °C
Log octanol–water partition coefficient	2.13

Organoleptic properties

Benzene has a characteristic odour. Its odour threshold in water is 10 mg/litre (*2*).

Major uses

Benzene is used in the chemical industry for the production of styrene/ethylbenzene, cumene/phenol, and cyclohexane (*1*). Its use as a solvent has been greatly reduced in the last few years (*3*). Benzene is used as an additive in petrol to increase the octane number (*2*).

Environmental fate

In soil, benzene biodegrades under aerobic conditions only. In surface water, it rapidly volatilizes to the air, biodegrades with a half-life of a few days to weeks, or reacts with hydroxyl radicals with a half-life of several weeks to months. In air, it reacts with hydroxyl radicals, with a half-life of about 5 days (*4*).

ANALYTICAL METHODS

Benzene can be determined by a purge-and-trap gas chromatographic procedure with photoionization detection, a method which is applicable over a concentration range of 0.02–1500 µg/litre. Confirmation is by mass spectrometry (detection limit 0.2 µg/litre) (*4*).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

Rural background concentrations of benzene, which may originate from natural sources (forest fire and oil seeps), have been reported to range from 0.3 to 54 µg/m^3. The general urban atmosphere reportedly contains 50 µg/m^3. In several studies conducted since 1963, average concentrations in ambient air ranged from 5 to 112 µg/m^3, mainly derived from vehicular emissions (*1*).

Exposure inside homes can occur from cigarette smoke or when houses are built on soil polluted with benzene. In one case, levels varying from 34 µg/m^3 (in the living space) up to

230 μg/m^3 (beneath the floor) were found. Benzene is found in the main stream (0.01–0.1 mg/cigarette) and in the side stream (0.05–0.5 mg/cigarette) of cigarette smoke (*3*). In a study in three states of the USA, weighted median concentrations were 9.8–16 μg/m^3 in indoor air and 0.4–7.2 μg/m^3 in outdoor air (*5*).

Water

The major sources of benzene in water are atmospheric deposition, spills of petrol and other petroleum products, and chemical plant effluents. Levels of up to 179 μg/litre have been reported in chemical plant effluents (*1*). In seawater, levels were reported to be in the range 5–20 ng/litre (coastal area) and 5 ng/litre (central part) (*3*). Levels between 0.2 and 0.8 μg/litre were reported in the Rhine in 1976) (*6*). Levels of 0.03–0.3 mg/litre were found in groundwater contaminated by point emissions (*7*).

Benzene was detected in 50–60% of potable water samples taken at 30 treatment facilities across Canada; mean concentrations ranged from 1 to 3 μg/litre (maximum 48 μg/litre) (*8*). Federal drinking-water surveys in the USA estimated that approximately 1.3% of all groundwater systems contained benzene at concentrations greater than 0.5 μg/litre (highest level reported 80 μg/litre) (*4*).

Food

Benzene may occur in food naturally, through migration from metallic covering layers of packaging material, or through contamination from the environment. It has been reported in several foods (eggs: 500–1900 μg/kg; rum: 120 μg/kg; irradiated beef: 19 μg/kg; heat-treated or canned beef: 2 μg/kg), and has also been detected in such foodstuffs as haddock, cheese, cayenne pepper, pineapple, and black currants (*9*).

Estimated total exposure and relative contribution of drinking-water

Exposure to benzene may vary considerably. For nonsmokers, the estimated average daily intake is 200–450 μg/day. The estimated contribution from food is 180 μg/day but, as information on benzene levels in food is very scanty, this background level should be considered only as an approximate reference point. For smokers, the intake levels are increased by a factor of 2–3 (urban areas) or 2–6 (rural areas). The levels commonly found in drinking-water are minimal compared with the intake from food and air (*3*).

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Benzene is rapidly and efficiently (30–50%) absorbed following inhalation. Following ingestion, animal data suggest about 100% absorption from the gastrointestinal tract. Less than 1% is absorbed through the skin. After absorption, benzene is widely distributed throughout the body, independently of the route of administration. Levels fall rapidly once exposure stops. Following uptake, adipose tissues have been found to contain high levels of benzene metabolites.

The metabolism and elimination of absorbed benzene appear to follow similar pathways in laboratory animals and humans. Benzene is converted mainly to phenol by the mixed-function oxidase system, primarily in the liver, but also in bone marrow. A small amount of phenol is metabolized to hydroquinone and catechol, and an even smaller amount is transformed into phenylmercapturic or *trans*-muconic acid. Between 12% and 14% (up to 50% in laboratory animals) of the absorbed dose is excreted unchanged in expired air. The respiratory elimination of benzene in humans is triphasic. In the urine, a small part is excreted unchanged, the remainder being excreted as phenol conjugates (*3,9–11*).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Benzene has a low acute toxicity. The oral LD_{50} in mice and rats is 1–10 g/kg of body weight; the 2.8-h LC_{50} is 15–60 g/m^3 (*3*).

Long-term exposure

Repeated exposure to low levels of benzene produces toxic effects principally in the blood and blood-forming tissues (*3*). Long-term exposure of mice to concentrations of 32–65 mg/m^3 results in inhibition of early differentiating blood cell elements (*12*).

In a study in which benzene was administered by gavage in corn oil 5 days per week for 103 weeks at doses of 0, 5, 100, or 200 mg/kg of body weight to F344/N rats or 0, 25, 50, or 100 mg/kg of body weight to B6C3F$_1$ mice, haematological effects, including lymphoid depletion of the splenic follicles (rats) and thymus (male rats), bone marrow haematopoietic hyperplasia (mice), lymphocytopenia, and associated leukocytopenia (rats and mice), were observed even at the lowest dose (*13–15*).

Reproductive toxicity, embryotoxicity, and teratogenicity

Benzene is not teratogenic even at maternally toxic doses. However, embryotoxicity/fetotoxicity was observed in rats and mice at levels as low as 65 mg/m^3 (*9*).

Mutagenicity and related end-points

Benzene was not mutagenic in several bacterial and yeast systems, in the sex-linked recessive lethal mutation assay with *Drosophila melanogaster*, or in the mouse lymphoma cell forward mutation assay. It can cause chromosome damage in plants and in mammalian somatic cells both *in vitro* and *in vivo*. Its clastogenic potential is partly due to its hydroxylated metabolites. Benzene and its metabolites may interfere with the formation of the mitotic spindle and perhaps do not interact directly with DNA. However, binding of benzene to nucleic acids has been reported (*3,10,15*).

Carcinogenicity

Benzene is carcinogenic in rats and mice after oral and inhalation exposure, producing malignant tumours at many sites. In a study by the National Toxicology Program, it was administered by gavage in corn oil 5 days per week for 103 weeks at doses of 0, 5, 100, or 200 mg/kg of body weight to F344/N rats and 0, 25, 50, or 100 mg/kg of body weight to B6C3F$_1$ mice. Compound-related non-neoplastic or neoplastic effects on the haematopoietic system, Zymbal gland, forestomach, and adrenal gland were seen in both sexes of both species. In addition, the oral cavity was affected in rats, and the lung, liver harderian gland, preputial gland, ovary, and mammary gland in mice (*13–15*).

EFFECTS ON HUMANS

Acute exposure of humans to high concentrations of benzene primarily affects the central nervous system. Acute exposure to 65 g/m^3 may cause death. Extensive haemorrhages have been observed in fatal cases (*3*).

Occupational exposure to more than 162 mg/m^3 results in toxic effects on the haematopoietic system, including pancytopenia. The white blood cells are the most sensitive (*10*).

There is considerable evidence that exposure to high benzene concentrations (=325 mg/m^3) may eventually result in leukaemia, in many cases preceded by pancytopenia or aplastic anaemia. Both epidemiological studies (*16,17*) and several case-studies showed that exposure to benzene was correlated with the occurrence of leukaemia (particularly acute myeloid leukaemia). Cytogenetic effects in peripheral lymphocytes were observed in human subjects with benzene haemopathy (*3,9,11,18*).

GUIDELINE VALUE

Benzene is carcinogenic in mice and rats after both inhalation and oral exposure, producing malignant tumours at many sites. It is considered to be a human carcinogen and is classified by IARC in Group 1 (*18*). Although it does not induce mutations or DNA damage in standard bacterial assay systems, it has been shown to cause chromosomal aberrations in a variety of species *in vivo*.

Because of the unequivocal evidence of the carcinogenicity of benzene in humans and laboratory animals and its documented chromosomal effects, quantitative risk extrapolation was used to estimate lifetime cancer risks. Based on a risk estimate using data on leukaemia from epidemiological studies involving inhalation exposure, it was calculated that a drinking-water concentration of 1 µg/litre was associated with an excess lifetime cancer risk of 10^{-6} (10 µg/litre is associated with an excess lifetime risk of 10^{-5} and 100 µg/litre with an excess lifetime risk of 10^{-4}) (*15*).

As data on the carcinogenic risk to humans following the ingestion of benzene are not available, risk estimates were also carried out on the basis of a 2-year gavage study in rats and mice (*13*). The robust linear extrapolation model was used, as there was a statistical lack of fit of some of the data with the linearized multistage model. The estimated range of concentrations in drinking-water corresponding to excess lifetime cancer risks of 10^{-4}, 10^{-5}, and 10^{-6}, based on leukaemia and lymphomas in female mice and oral cavity squamous cell carcinomas in male rats, are 100–800, 10–80, and 1–8 µg/litre, respectively. These estimates are similar to those derived from epidemiological data, which formed the basis for the previous guideline value of 10 µg/litre associated with a 10^{-5} excess lifetime cancer risk.

Guideline values corresponding to excess lifetime cancer risks of 10^{-4}, 10^{-5}, and 10^{-6} are therefore 100, 10, and 1 µg/litre, respectively.

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