

Xylenes 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.: 1130-20-7

Molecular formula: C₈H₁₀

The IUPAC name for xylene is dimethylbenzene. There are three possible xylene isomers: 1,2-, 1,3-, and 1,4-dimethylbenzene; these will be referred to as *o*- (ortho), *m*- (meta), and *p*- (para) xylene. The xylenes are for the most part manufactured and marketed as a mixture of the isomers, which will here be called xylene.

Physicochemical properties (1,2) [Conversion factor in air: 1 ppm = 4.41 mg/m³]

<i>Property</i>	<i>o-xylene</i>	<i>m-xylene</i>	<i>p-xylene</i>
Melting point (°C)	-25	-48	13
Boiling point (°C)	144.4	139.0	138.4
Vapour pressure at 25 °C (kPa)	0.906	1.11	1.17
Density at 20 °C (mg/litre)	0.88	0.86	0.86
Water solubility at 20 °C (mg/litre)	175	160	198 (25 °C)
Log octanol–water partition coefficient	2.77–3.12	3.20	3.15

Organoleptic properties

The lowest xylene concentrations in air reported to be perceptible to humans range from 0.6 to 16 mg/m³ (3,4). The odour threshold for xylene isomers in water is 0.02–1.8 mg/litre (4,5). Concentrations of 0.3–1.0 mg/litre in water produce a detectable taste and odour (6).

Major uses

Xylene is used in the manufacture of insecticides and pharmaceuticals, as a component of detergents, and as a solvent for paints, inks, and adhesives. Xylene-containing petroleum distillates are used extensively and increasingly in blending petrol. The three isomers are used individually as starting materials in the manufacture of various chemicals (1,2).

Environmental fate

Releases of xylene to the environment are largely to air because of its volatility; the calculated distribution of xylene is: air, 99.1%; water, 0.7%; soil, 0.1%; and sediment, 0.1% (7). Xylene degrades in air with a half-life of a few days. It is also readily biodegraded in soils and surface waters (2). Under aerobic conditions, it can be degraded in groundwater. Half-lives of from 24 to over 161 days have been reported (8,9). In anaerobic groundwater, no biotransformation is expected (10). When xylene is released to surface water, it volatilizes to air very rapidly.

ANALYTICAL METHODS

A purge-and-trap gas chromatographic procedure with photoionization detection can be used for the determination of xylene in water over a concentration range of 0.02–1500 µg/litre (11). Confirmation is by mass spectrometry (12). Methods for the determination of xylene in air, soil, and other matrices have been reviewed and compiled by Fishbein & O'Neill (13).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

Mean atmospheric concentrations of xylene in urban areas around the world range from 3 to 390 $\mu\text{g}/\text{m}^3$ (1). Outdoor concentrations of 0.6–61 $\mu\text{g}/\text{m}^3$ have been reported in the USA (1,14). Concentrations of 100 $\mu\text{g}/\text{m}^3$ were found at cross-roads (1). Indoor air concentrations range from 5.2 to 29 $\mu\text{g}/\text{m}^3$ and are higher (200 $\mu\text{g}/\text{m}^3$) in the presence of cigarette smoke. The average ratio of indoor to outdoor air concentration is 1.2 for *m*-xylene and 4.0 for *o*-xylene (15).

Water

Xylene has been found at levels of 2–8 $\mu\text{g}/\text{litre}$ in the surface water of Florida Bay (16). In the Netherlands section of the Rhine, the average xylene concentration in 1987 was 0.3 $\mu\text{g}/\text{litre}$ (0.1 $\mu\text{g}/\text{litre}$ for each isomer); the maximum value was 1.2 $\mu\text{g}/\text{litre}$. In the surface water of Lake IJsselmeer, the average and maximum concentrations were 0.3 and 0.9 $\mu\text{g}/\text{litre}$, respectively (17).

In groundwater contaminated by point emissions, xylene levels of 0.3–5.4 mg/litre have been reported; levels in uncontaminated groundwater are low (<0.1 $\mu\text{g}/\text{litre}$) (18). The highest level in groundwater in the USA (1983) was 2.5 $\mu\text{g}/\text{litre}$ (2). In the Netherlands, xylene was detected in 10.1% of 304 samples of groundwater used for potable water production; the maximum concentration found was 0.7 $\mu\text{g}/\text{litre}$ (19).

Xylene levels in approximately 3% of all groundwater-derived public drinking-water systems and 6% of all surface-water-derived drinking-water systems in the USA were greater than 0.5 $\mu\text{g}/\text{litre}$, the maximum level being 5.2 $\mu\text{g}/\text{litre}$ (2). In Canada, *m*-xylene was found in seven out of 30 potable water treatment plants at concentrations below 1 $\mu\text{g}/\text{litre}$ (20). In Ontario, xylene was found in drinking-water at concentrations of less than 0.5 $\mu\text{g}/\text{litre}$ (21). In drinking-water and tapwater in New Orleans, concentrations of 3–8 $\mu\text{g}/\text{litre}$ were reported (16). Concentrations in drinking-water can be increased by the leaching of xylene from the synthetic coating materials commonly used to protect the tanks used for its storage (22).

Estimated total exposure and relative contribution of drinking-water

Because of the low levels of xylene reported in drinking-water, air is likely to be the major source of exposure. If a mean ventilation volume of 20 m^3/day (75% indoor air; 25% outdoor air) and an absorption of 65% are assumed, the daily exposure can be estimated to range from 0.05 to 0.5 mg. This exposure will be increased when air is polluted with cigarette smoke.

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Data on absorption after ingestion are not available. Xylene isomers are readily absorbed after inhalation, with retention percentages of 60–65% in humans. They are absorbed to some extent (exact percentages not known) via the skin; the few data available indicate rapid distribution of the compound after uptake. Xylenes can cross the placenta. They are stored in adipose tissue in both laboratory animals and humans. A small part (< 5%) of the absorbed amount is exhaled unchanged; the remainder is converted almost quantitatively to methyl benzoic acid, which is excreted in urine as methyl hippuric acid. Few data on rates of excretion are available; it is eliminated from subcutaneous fat in humans with a half-life ranging from 25 to 128 h (2,7,23).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Xylene isomers have a low acute toxicity via the oral route; LD₅₀s in rats range from 3.6 to 5.8 g/kg of body weight (1).

Short-term exposure

Available short-term oral studies are of limited design. The toxicological significance of the ultrastructural liver changes observed in rats (24) at the only dose level tested (200 mg of *o*-xylene per kg of feed) is questionable given the absence of any histopathological signs in the livers of rats tested at much higher dose levels in oral studies carried out under the US National Toxicology Program (25). In addition, the results of the single-dose study are presented only for the group of methylated benzenes tested; the results observed with the individual compounds are not reported. In inhalation studies in rats, liver enzyme induction was observed at concentrations of 217 mg/m³ and above, 6 h per day (NOAEL not determined) (23,26).

Long-term exposure

A carcinogenicity study in rats and mice provided some relevant information on the toxic effects of xylenes after oral administration. In rats, 0, 250, or 500 mg/kg of body weight per day was administered by gavage in corn oil, 5 days per week for 103 weeks. Growth was decreased at 500 mg/kg of body weight per day; no compound-related histological lesions were observed. The NOAEL for rats was 250 mg/kg of body weight per day. In mice, the dose levels tested were 0, 500, and 1000 mg/kg of body weight per day. The only observed effect in this species was hyperactivity at 1000 mg/kg of body weight per day (25).

Reproductive toxicity, embryotoxicity, and teratogenicity

Both of the oral studies carried out in mice showed maternal toxicity with concurrent embryotoxicity and teratogenicity (increased incidence of cleft palate) at the higher dose levels tested (LOAEL 640 mg/kg of body weight; NOAEL 255 mg/kg of body weight) (27,28). Teratogenicity studies carried out in rats and mice by the inhalation route showed maternal toxicity at high dose levels but no teratogenicity (7,23).

Mutagenicity and related end-points

The mutagenic activity of xylenes was examined in bacteria and in mammalian cells (both *in vitro* and *in vivo*) with negative results. The significance of a weak positive effect observed with technical xylene in a *Drosophila* recessive lethal test is not clear, given the negative results in the same test system obtained with the individual components of the technical mixture (7,23,29).

Carcinogenicity

An oral carcinogenicity study in rats (0, 250, or 500 mg/kg of body weight per day administered by gavage in corn oil, 5 days per week for 103 weeks) and mice (0, 500, or 1000 mg/kg of body weight per day) did not show xylenes to be carcinogenic (25).

EFFECTS ON HUMANS

No oral data are available. In acute inhalation studies, irritation of eyes and throat was observed at concentrations of 480 mg/m³ and above. After short-term exposure (6 h per day, 5

days per week), reaction time, manual coordination, body equilibrium, and electroencephalogram were affected at concentrations of 390 mg/m³ and above (NOAEL not determined). Controlled studies of longer duration are not available (7,23).

GUIDELINE VALUE

On the basis of the available evidence, xylenes should not be regarded as initiating carcinogens, so that a TDI approach may be used. A TDI of 179 µg/kg of body weight was derived using a NOAEL of 250 mg/kg of body weight per day based on decreased body weight in a 103-week gavage study in rats (25) with administration 5 days per week (equivalent to 179 mg/kg of body weight per day 7 days per week) and an uncertainty factor of 1000 (100 for intra- and interspecies variation and 10 for the limited toxicological endpoint). This TDI yields a guideline value of 500 µg/litre (rounded figure), allocating 10% of the TDI to drinking-water. This value, however, exceeds the lowest reported odour threshold for xylenes in drinking-water of 20 µg/litre.

REFERENCES

1. International Agency for Research on Cancer. *Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting*. Lyon, 1990:125-126 (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 47).
2. US Environmental Protection Agency. USEPA Office of Drinking Water health advisories. *Reviews of environmental contamination and toxicology*, 1988, 106:189-203.
3. Agency for Toxic Substances and Disease Registry. *Toxicological profile for xylenes*. Atlanta, GA, Department of Health and Human Services, 1990.
4. Van Gemert LJ, Nettenbrijer AH, eds. *Compilation of odour threshold values in air and water*. Zeist, Netherlands, National Institute for Water Supply/Central Institute for Nutrition and Food Research TNO, 1977.
5. Verschueren K. *Handbook of environmental data on organic chemicals*, 2nd ed. New York, NY, Van Nostrand Reinhold Company, 1983:1188-1195.
6. Middleton FM, Rosen AA, Burtschell RH. Taste and odor research tools for water utilities. *Journal of the American Water Works Association*, 1958, 50:21-28.
7. European Chemical Industry Ecology and Toxicology Centre. *Joint assessment of commodity chemicals No. 6: Xylenes CAS: 95-47-6(o), 108-38-3(m), 106-42-2(p), 1330-20-7(mixture)*. Brussels, 1986.
8. Barker JF et al. The organic geochemistry of a sanitary landfill leachate plume. *Journal of contaminant hydrology*, 1986, 1:171-189.
9. Wilson JT et al. Relationship between the ATP content of subsurface material and the rate of biodegradation of alkylbenzenes and chlorobenzene. *Journal of contaminant hydrology*, 1986, 1:163-170.
10. Wilson JT et al. Biotransformation of selected organic pollutants in groundwater. *Developments in industrial microbiology*, 1983, 24:225-233.
11. Environmental Monitoring and Support Laboratory. *Method 503.1. Volatile aromatics and unsaturated organic compounds in water by purge and trap gas chromatography*. Cincinnati, OH, US Environmental Protection Agency, 1985.
12. Environmental Monitoring and Support Laboratory. *Method 524.1. Volatile organic compounds in water by purge-and-trap gas chromatography/mass spectrometry*. Cincinnati, OH, US Environmental Protection Agency, 1985.
13. Fishbein L, O'Neill IK, eds. *Environmental carcinogens: methods of analysis and exposure measurement*. Vol. 10. *Benzene and alkylated benzenes*. Lyon, International Agency for Research on Cancer, 1988 (IARC Scientific Publications No. 85).
14. Wallace LA. The TEAM Study: personal exposures to toxic substances in air, drinking-water, and breath of 400 residents of New Jersey, North Carolina, and North Dakota. *Environmental research*, 1987, 43:290-307.

15. Montgomery DD, Kalman DA. Indoor/outdoor air quality: reference pollutant concentrations in complaint-free residences. *Applied industrial hygiene*, 1989, 4:17-20.
16. Merian E, Zander M. Volatile aromatics. In: Hutzinger O, ed. *Handbook of environmental chemistry*. Vol. 3, Part B. *Anthropogenic compounds*. Berlin, Springer, 1982:117-161.
17. *De samenstelling van het Rijnwater in 1986 en 1987*. [The composition of the water of the Thine in 1986 and 1987.] Amsterdam, Netherlands, RIWA (Rhine and Maas Waterworks Association), 1989.
18. Department of the Environment. *Environmental hazard assessment: xylenes*. Garston, Building Research Establishment, 1993.
19. Veenendaal G, van Beek CGEM, Puyker LM. *Het voorkomen van organische stoffen in het grondwater onttrokken door de Nederlandse Waterleidingbedrijven*. [The occurrence of organic compounds in groundwater withdrawn by the Netherlands water-supply undertakings.] KIWA (Netherlands Waterworks Testing and Research Institute), 1986 (KIWA Report No. 97).
20. Otson R, Williams DT, Bothwell PD. Volatile organic compounds in water in thirty Canadian potable water treatment facilities. *Journal of the Association of Official Analytical Chemists*, 1982, 65:1370-1374.
21. Smillie RD, Sakuma T, Duholke WK. Low molecular weight aromatic hydrocarbons in drinking water. *Journal of environmental science and health*, 1978, A13(2):187-191.
22. Bruchet A, Shipert E, Alben K. Investigation of organic coating material used in drinking water distribution systems. *Journal français d'hydrologie*, 1988, 19:101-111.
23. Janssen P, Van der Heijden CA, Knaap AGAC. [Short summary and evaluation of toxicological data on xylene.] Bilthoven, Netherlands, National Institute of Public Health and Environmental Protection, 1989 (in Dutch).
24. Bowers DE, Cannon MS, Jones DH. Ultrastructural changes in livers of young and aging rats exposed to methylated benzenes. *American journal of veterinary research*, 1982, 43:679-683.
25. National Toxicology Program. *Toxicology and carcinogenesis studies of xylenes (mixed) (60% m-xylene, 14% p-xylene, 9% o-xylene, 17% ethylbenzene) (CAS No. 1330-20-7) in F344/N rats and B6C3F₁ mice (gavage studies)*. Research Triangle Park, NC, 1986 (NTP Technical Report Series No. 327).
26. US Environmental Protection Agency. USEPA Office of Drinking Water health advisories. *Reviews of environmental contamination and toxicology*, 1987, 106:213-222.
27. Marks TA, Ledoux TA, Moore JA. Teratogenicity of a commercial xylene mixture in the mouse. *Journal of toxicology and environmental health*, 1982, 9:97-105.
28. Nawrot PS, Staples RE. Embryofetal toxicity and teratogenicity of isomers of xylene in the mouse. *Toxicologist*, 1981, 1:A22.
29. Donner M et al. Genetic toxicology of xylenes. *Mutation research*, 1980, 74:171-172.