Exh. RXS-16

US EPA, Health Effects Notebook for Hazardous Air Pollutants, Xylenes

(Publicly available at https://www.epa.gov/sites/default/files/2016-09/documents/xylenes.pdf)

Xylenes (A) (Mixed Isomers)

o-XYLENE
m-XYLENE
p-XYLENE

1330-20-7, 95-47-6, 108-38-3, 106-42-3

Hazard Summary

Commercial or mixed xylene usually contains about 40-65% m-xylene and up to 20% each of o-xylene and p-xylene and ethylbenzene. Xylenes are released into the atmosphere as fugitive emissions from industrial sources, from auto exhaust, and through volatilization from their use as solvents. Acute (short-term) inhalation exposure to mixed xylenes in humans results in irritation of the eyes, nose, and throat, gastrointestinal effects, eye irritation, and neurological effects. Chronic (long-term) inhalation exposure of humans to mixed xylenes results primarily in central nervous system (CNS) effects, such as headache, dizziness, fatigue, tremors, and incoordination; respiratory, cardiovascular, and kidney effects have also been reported. EPA has classified mixed xylenes as a Group D, not classifiable as to human carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (6), which contains information on oral chronic toxicity and the RfD, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Xylenes. (1)

Uses

- Mixed xylenes are used in the production of ethylbenzene, as solvents in products such as paints and coatings, and are blended into gasoline. (1)

Sources and Potential Exposure

- Mixed xylenes are distributed throughout the environment; they have been detected in air, rainwater, soils, surface water, sediments, drinking water, and aquatic organisms. (1)
- Xylenes are released into the atmosphere as fugitive emissions from industrial sources, from auto exhaust, and through volatilization from their use as solvents. (1)
- Ambient air concentrations of mixed xylenes in urban areas of the United States range from 0.003 to 0.38 milligrams per cubic meter (mg/m^3). (1)
- Mixed xylenes have also been detected at low levels in indoor air; xylenes have been widely used in home use products such as synthetic fragrances and paints. One study reported concentrations of m- and p-xylene ranging from 0.010 to 0.047 mg/m^3. (1)
- Levels of mixed xylenes in drinking water have been reported to range from 0.2 to 9.9 micrograms per liter (µg/L), with mean concentrations of less than 2 µg/L. (1)
- Occupational exposure to mixed xylenes may occur at workplaces where mixed xylenes are produced and used as industrial solvents. (1)
- Xylene exposure may be to any of the three isomers or to mixtures of the isomers. (1)

Assessing Personal Exposure

- Exposure to mixed xylenes may be determined by measuring the breakdown products of mixed xylenes in the urine or by measuring levels of xylene in blood or exhaled breath. (1)

Health Hazard Information

Acute Effects:

- Human and animal data show that all xylene isomers or xylene mixtures produce similar effects, although specific isomers may not be equally potent in producing the effects. (1)
- Acute inhalation exposure to mixed xylenes in humans has been associated with dyspnea and irritation of the nose and throat; gastrointestinal effects such as nausea, vomiting, and gastric discomfort; mild transient eye irritation; and neurological effects such as impaired short-term memory, impaired reaction time, performance decrements in numerical ability, and alterations in equilibrium and body balance. (1-3)
- Acute dermal exposure in humans results in transient skin irritation and dryness and scaling of the skin. (1-3)
- Acute inhalation exposure to a mixture of toluene and xylenes resulted in more than additive respiratory and neurological toxicity in humans and animals. (1)
- Acute animal studies have reported respiratory, cardiovascular, CNS, liver, and kidney effects from inhalation exposure to mixed xylenes. (1)
- Acute animal tests in rats and mice have shown mixed xylenes to have low to moderate toxicity from inhalation exposure and moderate toxicity from oral exposure. (4,5)

Chronic Effects (Noncancer):

- Chronic exposure of humans to mixed xylenes, as seen in occupational settings, has resulted primarily in neurological effects such as headache, dizziness, fatigue, tremors, incoordination, anxiety, impaired short-term memory, and inability to concentrate. Labored breathing, impaired pulmonary function, increased heart palpitation, severe chest pain, abnormal EKG, and possible effects on the kidneys have also been reported. (1,2)
- Mixed xylenes have not been extensively tested for chronic effects, although animal studies show effects on the liver and CNS from inhalation and oral exposures and effects on the kidneys from oral exposure to mixed xylenes. (1)
- The Reference Dose (RfD) for mixed xylenes is 2 milligrams per kilogram body weight per day (mg/kg/d) based on hyperactivity, decreased body weight, and increased mortality in rats, and the provisional RfD for m- and o-xylenes is also 2 mg/kg/d. EPA has not established an RfD for p-xylene. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. The provisional RfDs are values that have had some form of Agency review, but do not appear on IRIS. (6,10)
- EPA has medium confidence in the study on which the RfD was based because it was a well-designed study in which adequately sized groups of two species were tested over a substantial portion of their lifespan, comprehensive histology was performed, and a no-observed-adverse-effect level (NOAEL) was defined; but clinical chemistries, blood enzymes, and urinalysis were not performed; medium confidence in the database because although supporting data exist for mice, and teratogenicity and fetotoxicity data are available with positive results at high oral doses, a lowest-observed-adverse-effect level (LOAEL) for chronic oral exposure has not been defined; and, consequently, medium confidence in the RfD. (6)
- EPA has not established a Reference Concentration (RfC) for mixed xylenes or any isomers. (6)
- ATSDR has calculated a chronic inhalation minimal risk level (MRL) of 0.4 mg/m^3 (0.1 parts per million [ppm]) for mixed xylenes based on neurological effects in occupationally exposed workers. The MRL is an

estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- Several human studies examined exposure to organic solvents (including mixed xylenes) and developmental effects. An increased potential for spontaneous abortions among the wives of occupationally exposed men was reported. However, no conclusions can be drawn from these studies because they all involved concurrent exposure to multiple chemicals. (1)
- Mixed xylenes have been shown to produce developmental effects, such as an increased incidence of skeletal variations in fetuses, delayed ossification, fetal resorptions, and decreased fetal body weight in animals via inhalation exposure. Some studies observed maternal toxicity as well. (1-3)

Cancer Risk:

- No information is available on the carcinogenic effects of mixed xylenes in humans. (1)
- An increase in tumors was not reported in rats or mice exposed to mixed xylenes via gavage (experimentally placing the chemical in the stomach). Other animal studies have reported equivocal results. (1,3,6)
- EPA has classified mixed xylenes as a Group D, not classifiable as to human carcinogenicity. (6)

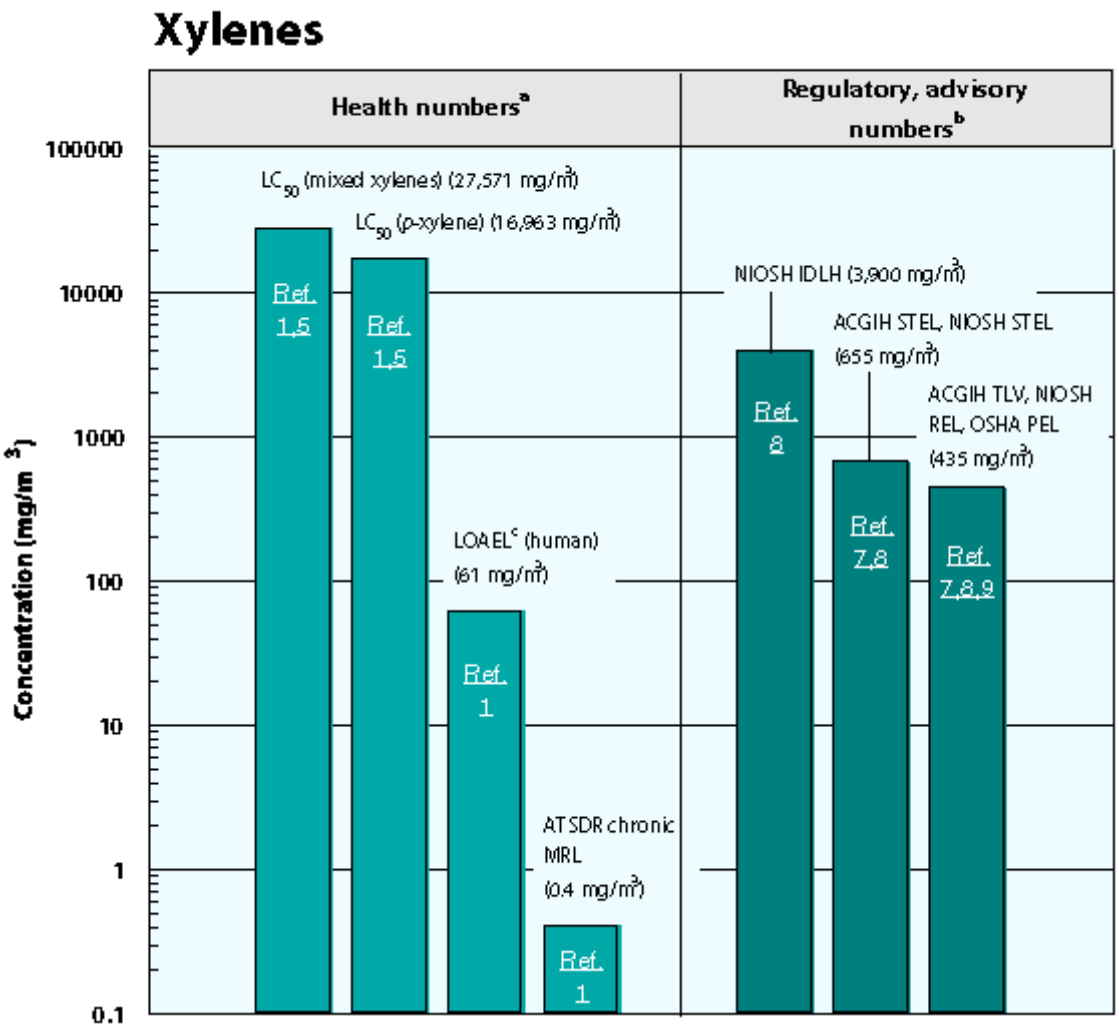
Physical Properties

- m-, o-, and p-Xylene are the three isomers of xylene; commercial or mixed xylene usually contains about 40-65% m-xylene and up to 20% each of o- and p-xylene and ethylbenzene. (1)
- Mixed xylenes are colorless liquids that are practically insoluble in water and have a sweet odor. (1)
- The odor threshold for m-xylene is 1.1 ppm. (4)
- The chemical formula for mixed xylenes is C_8H_{10}, and the molecular weight is 106.16 g/mol. (1)
- The vapor pressure for mixed xylenes is 6.72 mm Hg at 21 °C, and the log octanol/water partition coefficient ($\log K_{ow}$) is 3.123.20. (1)

Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m^3: $mg/m^3 = (ppm) \times (\text{molecular weight of the compound})/(24.45)$. For xylenes: 1 ppm = 4.34 mg/m^3. To convert concentrations in air from $\mu g/m^3$ to mg/m^3: $mg/m^3 = (\mu g/m^3) \times (1\ mg/1{,}000\ \mu g)$.

Health Data from Inhalation Exposure



ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

ACGIH TLV--ACGIH's threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration $_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL-- Lowest observed adverse effect level.

NIOSH IDLH -- National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

NIOSH REL--NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH STEL--NIOSH's recommended short-term exposure limit; a 15-minute TWA exposure which should not be exceeded at any time during a workday.

OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

The health and regulatory values cited in this factsheet were obtained in December 1999.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

[b]

[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

[c] This LOAEL is from the critical study used as the basis for the ATSDR chronic inhalation MRL.

Summary created in April 1992, updated in January 2000

References

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A. * This fact sheet refers to the mixture of all three isomers of mixed xylenes as "mixed mixed xylenes" and the isomers by their individual isomer names.