Benzene exposure and cancer. Scientific evidence and regulatory development
Highlights from yesterday's expert seminar

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Petroleum Safety Authority 25 October 2018

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Concluding the expert seminar: Benzene exposure and related cancer risk in the oil and gas industry – scientific evidence, regulatory processes, and management practices

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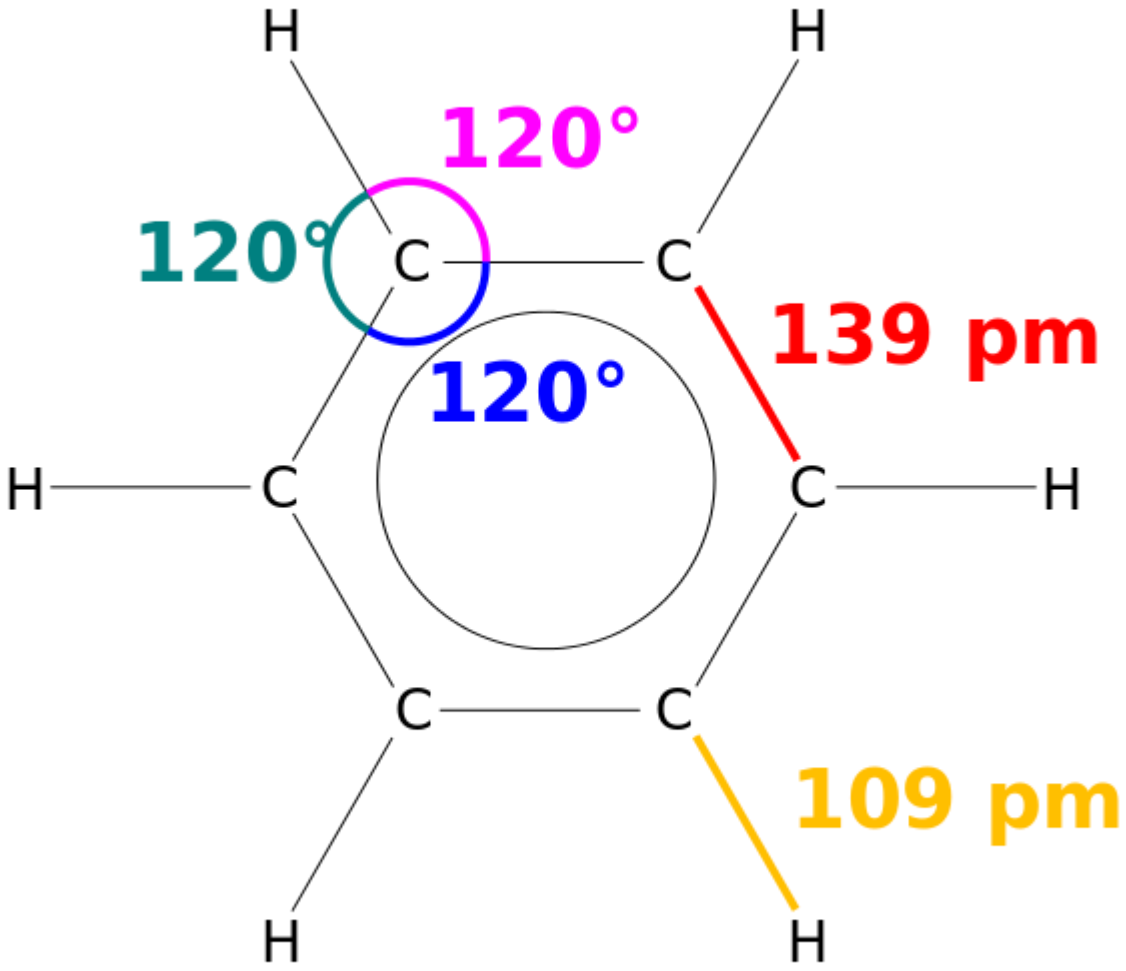
Benzene, bp 80°C, density 0.88, solubility in water 1.8 g/l



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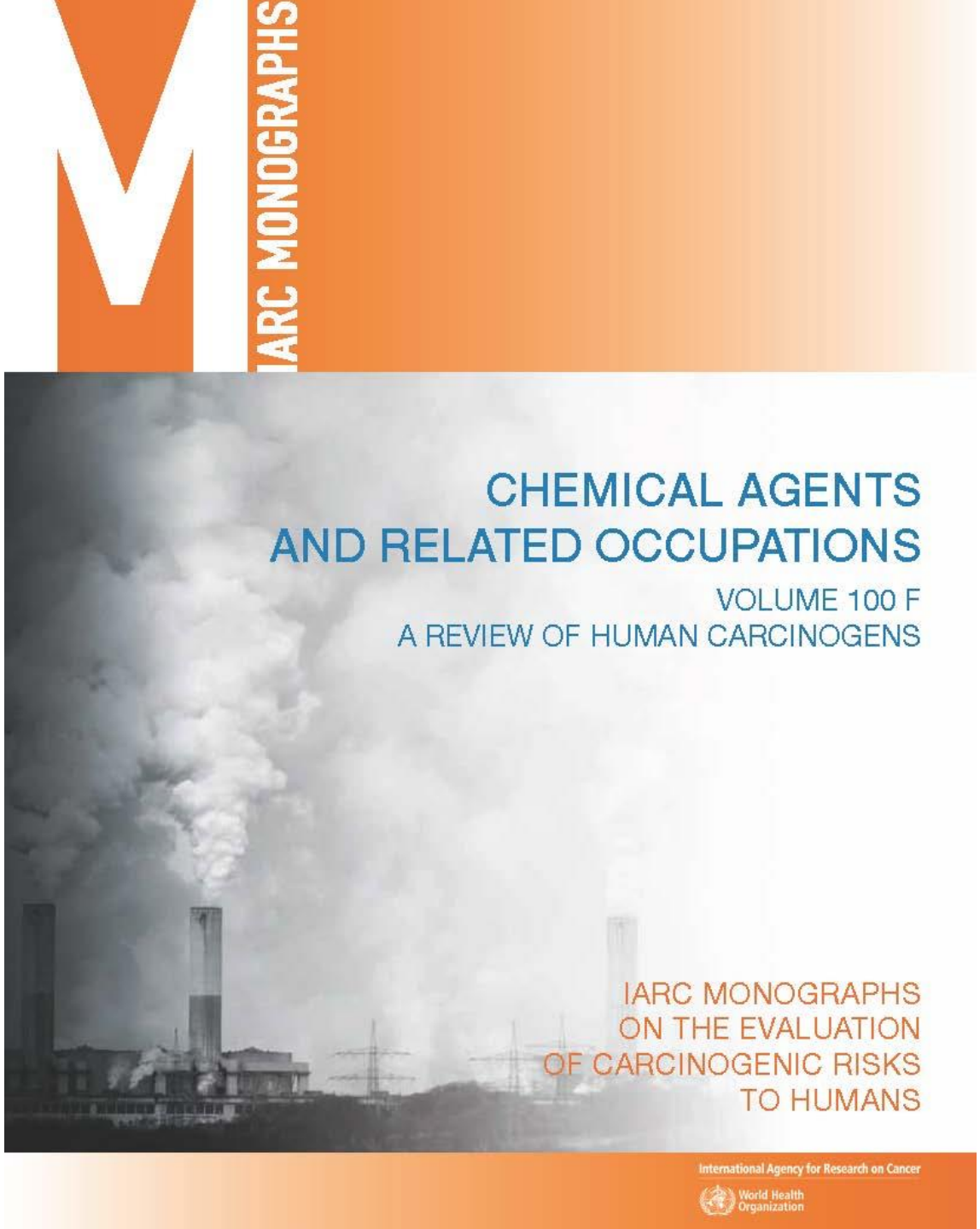
IARC Monographs on benzene:
1974 (vol 7)
1982 (vol 29)
1987 (suppl 4)
1987 (suppl 7)
2009 (vol 100F)
2019(?) (vol 120)

Carcinogenic risk to humans from benzene exposure



Occupational exposure to benzene

- Causes Acute Myelogenous Leukemia (IARC 1982)
  - Within 10 (-15) years after end of exposure (Triebig 2010)
- Is positively associated with Non-Hodgkin lymphoma (Vlaanderen *et al.* 2011, IARC 2012) including
  - Acute Lymphocytic Leukemia
  - Chronic Lymphocytic Leukemia
  - Multiple Myeloma

Classification of NHL has changed dramatically in recent years – see e.g. Swerdlow (IARC), 2008

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Exposure to benzene

- Inhalation or dermal exposure
  - Occupational exposure is defined as inhalation or dermal exposure at work to benzene likely to exceed significantly non-occupational exposure due to inhaling urban air or filling in gasoline stations (long-term exposure usually below 0.01 ppm) (IARC 2012)

Groups potentially exposed to benzene in the Norwegian petroleum industry

- 14 occupational groups assessed by expert group (Steinsvåg et al, 2008): considered exposed from 1970 - 2005
  - Mechanics
  - Electricians
  - Electric instrument technicians
  - Piping engineers and inspectors
  - Laboratory enginieers and inspectors
  - Process technicians
  - Insulators
  - Industrial cleaners
  - Painters (1970-1989 only)

  - Additionally process operators were considered exposed to skin contact with crude oil

  - About 30 % of the offshore workers cohort (CRN 2006) were considered exposed to benzene
  - According to NOA / STAMI 24 % of workers in exploitation of crude oil / natural gas reported that they are exposed to chemicals/gas/vapours

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Health effects, benzene exposure

- Carcinogenicity (AML, MDS, NHL, Lung?) threshold or not?
- Haematogical (LOAEC 2 ppm?)
- Immunological (at similar levels of exposure as hematological)
- Irritancy, corrosivity
- Sensitisation
- Genotoxicity (chromosome aberrations, aneuploidy, micronuclei) in the concentration range of 0.1-1 ppm
- Epigenetic alterations (DNA methylation, histone modifications, non-coding RNA)
- Neurological (at high levels of inhalation exposures, 300-3000 ppm)
  - Neuropathy, Sleep disturbances, Memory difficulties

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Aims for the measurement technology, evaluating compliance with a suggested level <0.05 ppm

- Level of quantification should be below 1/10 of the OEL (0.005 ppm if new OEL is 0.05 ppm) regarding sources of variation both from sampling and analysis
- Active air sampling using a tube with charcoal absorbent or thermo desorption tube; and analysis by GC-MS may provide this low LOQ for both 8 hr and short time sampling intervals down to 5 min
- Diffusive sampling may also be useful at 8 hrs sampling time, but probably not for short sampling intervals
- Direct-reading PID instruments are available, but yet probably not with sufficiant specificity for benzene or adequately low LOQ to assess 5 ppb

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Present level of quantification LOQ

- Benzene in air (active sampling for short-term): sub-ppb level for 8 hrs, <5 ppb for 15 min
- Benzene in air (passive sampling): <5 ppb
- SPMA in urine (reflects past day exposure) 0.3 ppm in 8 hrs; STAMI preliminary results (20-27 min exposure time) detects a level of ~0.025 ppm benzene measured as SPMA in dilute urine, 4 µg SPMA/g creatinine in urine)
- Benzene in urine: 0.03 ppm 8 hrs in non-smokers
- Benzene in blood: (ref Peter Boogaard)

Benzene in urine prone to loss due to volatility, less problem with benzene in urine)

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Biological limit values (DFG 2017)

- 0.7 µg benzene/L urine and
- 2 µg SPMA/g creatinine in urine (sampled at the end of the shift)

- Biological guidance value
  - 0.3 µjg benzene/L urine
  - 0.5 µg SPMA/g creatinine in urine
  - 150 µg tt muconic acid / g creatinine (~suitable to monitor levels > 1ppm?)

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Background levels of benzene in the population (95 percentiles), suggested BGV biological guidance values (suitable to monotor exposure to >0.03 ppm benzene in ambient air

- Benzene in urine 0.3 µg /L
- SPMA in urine 0.5 µg /g creatinine

Not suited as biomarkers of benzene exposure at a level < 1 ppm

- Phenol (suitable > 8 ppm?)
- Hydroquinone
- Catechol

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Which are the highest exposed tasks offshore?

- Tasks with highest short-term exposure (median > 1 ppm)
  - Flotation
  - Maintenance/filter work
  - Cleaning tasks, e.g. plate separator
- Tasks with highest long-term exposure (median > 0.1 ppm)
  - Cleaning of separator, tank (38% of individual meas > 0.6 ppm, N=26 samples)
  - Pigging

Bråtveit *et al.* 2010

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Which are the highest exposed tasks onshore?

- Tasks with highest short-term exposure (median > 1 ppm)
  - Sampling of fuels
- Tasks with highest long-term exposure (median > 0.1 ppm)
  - Opening of hydrocarbon containing systems
  - Purification system work (renseanlegg) especially in the year 1989

Bråtveit *et al.* 2010

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Inhalational exposure – the whole story?

- Heavy physical exertion at work – increase of ventilation of the lungs
- Metabolism of benzene may be affected by co-exposure to other solvents – modifying its toxicity
- Skin uptake – very little is known and no measurement data of relevance have been identified
  - Intact skin is permeable to benzene – an uptake rate of 0.4 mg/cm^2*h was found (Hanke *et al.* 1961)
  - Damaged skin may possibly be more permeable and uptake may possibly be affected by co-application of other solvents or water
  - Clothes covering spills containing benzene on the skin occluding the contamination may be speculated to let more benzene be absorbed and less to evaporate

A targeted risk reduction/ exposure reduction depends on more knowledge of the exposure levels as well as new data on possible harmful levels of exposure

- Present and historical levels of exposure are described with a high degree of uncertainty
- Levels of allowed occupation exposure are under consideration in light of the new scientific information that has emerged during the last 10 years
- More measurements with relevant contextual information are needed, and groups with a high variability in exposure level with time need more sampling days per worker in order to conclude about the typical levels of exposure to benzene and their variation
- More information on within-worker variance could enable more targeted exposure reduction activities

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