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Evaluation of Worker Exposure to Benzene

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Benzene is recognized as a human carcinogen (leukemogen) by the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the International Agency for Research on Cancer. An estimated 2-3 million workers are potentially exposed to benzene (ATSDR 1989). It is important to have cancer risk factors available for the evaluation of worker exposures in various settings. The risk factors for benzene published by the EPA are designed to evaluate general population exposure (not worker exposure) and do not include the results of recent studies. In this paper, risk factors are derived for the evaluation of worker cancer risk due to the inhalation and ingestion of benzene. These cancer risk factors are characterized by route, species, strain, sex, dose, dose rate/kg, and fraction of lifetime exposed. Such characterization facilitates the matching of a risk factor to any exposure situation. Example applications of the risk factors are presented. These examples concern OSHA's permissible exposure limit (PEL) for benzene, inhalation exposure at leaking underground gasoline storage tank sites (LUSTs), and ingestion of contaminated soil.

MATERIALS AND METHODS

Cancer risk factors are usually derived from experimental studies in units of excess risk/(mg/m^3) or excess risk/(mg/kg/day). Experimental studies can be animal or epidemiologic. In order to obtain a risk factor, it is first necessary to compute excess risk and equivalent human dose from an experimental study. Excess risk is the frequency of response in the exposed group corrected for the control group response. The equivalent human dose from an animal or epidemiology study is a function of the following variables: pharmacokinetics; body weight (or surface area); exposure concentration; daily

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intake of contaminated air, food, or water; exposure period; time of observation from last exposure; lifespan; and latent period. See Hallenbeck and Cunningham (1986) for a discussion of the calculation of excess risk and equivalent human dose.

RESULTS and DISCUSSION

Of several published epidemiology studies, only two (Rinsky et al 1987; Wong 1987) were deemed suitable for the determination of cancer risk factors for the inhalation of benzene. These inhalation risk factors are characterized in Table 1.

Table 1. Cancer risk factors for benzene inhalation (derived from epidemiology studies)

Risk factor characteristics				Risk factors for workers	
Ref	Dose rate (mg/kg/d)	Frac[a]	Dose ($mgx10^6$)	$[(mg/m^3)^{-1} \times 10^{-4}]$[b]	$(mg/kg/d)^{-1}$ [c]
Rinsky 1987	22.8	0.15	5.1	3.5	0.0024
Rinsky 1987	22.8	0.15	5.1	4.6	0.0032
Wong 1987	1.37	0.12	0.24	32	0.022
Wong 1987	1.37	0.12	0.24	19	0.013
Wong 1987	1.37	0.12	0.24	35	0.024

[a] Frac = fraction of lifetime exposed
[b] Assumes an intake of 10 m^3/day of contaminated air over 250 days/year and 45 years.
[c] Assumes 70 kg body weight and exposure over 250 days/year and 45 years.

There were several potentially confounding factors regarding the exposure estimates in the Rinsky et al (1987) study. The exposure history of some of the workers was based on past industrial hygiene measurements taken primarily from only one of two exposure locations. Also, early measurements were made with sampling devices of questionable accuracy. Finally, workers were exposed to several chemicals.

The cohort studied by Wong (1987) also was exposed to

several chemicals. To control for their effect, workers exposed to chemicals with the exception of benzene were used as the comparison group.

Skin absorption of benzene is an unmeasured factor in occupational epidemiology studies. Workers were exposed to benzene vapor and probably had direct skin contact with liquid. Workers used benzene to clean hands, clothing, and tools, both at home and work (DeCoufle et al 1983). If epidemiologic risk factors are used, it is highly likely that dermal exposure and response are at least partially taken into account by the inhalation risk factor.

Several animal inhalation studies were deemed suitable for the determination of cancer risk factors for inhaled benzene. These inhalation risk factors are characterized in Table 2.

One animal ingestion study was deemed suitable for the determination of cancer risk factors for ingested benzene. These ingestion risk factors are characterized in Table 3.

Theoretical lifetime excess cancer risk refers to a calculated probability (risk) of dying of cancer due to exposure to a carcinogen over a working lifetime (45 years). In order to calculate theoretical lifetime excess risk, exposure characteristics (dose, fraction of lifetime exposed, and dose rate/kg) must be calculated for a particular worker group. An appropriate risk factor can then be selected from Tables 1,2, or 3 by matching, as closely as possible, the exposure conditions of the worker group and the experimental group. Any two of the three parameters (dose, dose rate/kg, and fraction of lifetime exposed) will completely specify the conditions of exposure, since the third parameter is fixed by the other two. Risk factors based on epidemiological data are preferred if the worker and experimental exposure characteristics match. If worker exposure conditions do not match those for a risk factor developed from epidemiological data, a risk factor based on animal data may be selected.

In the following example, assume worker exposure at the current OSHA PEL of 1 ppm (3.2 mg/m^3) over 250 days/year and 45 years and an intake of contaminated air of 10 m^3/day. First, calculate worker dose, dose rate/kg, and fraction of lifetime exposed.

Dose = 3.2 mg/m^3 x 10 m^3/d x 250 d/yr x 45 yr

= 3.6×10^5 mg

Table 2. Cancer risk factors for benzene inhalation (derived from animal studies)

Risk factor characteristics						Risk factors for workers	
Ref	Dose rate (mg/kg/d)	Frac[a]	Dose (mgx10^7)	Sp[b]	Sex	[$(mg/m^3)^{-1}$ x 10^{-4}][c]	$(mg/kg/d)^{-1}$ [d]
Snyder 1980	320	0.5	23	m	M	1.9	0.0013
Cronkite 1985	383	0.16	6.8	m	F	3.3	0.0023
Cronkite 1986,89	107	0.02	1.2	m	M	51	0.035
Cronkite 1986,89	320	0.1	4.9	m	M	9.6	0.0067
Cronkite 1986,89	320	0.1	4.9	m	M	18	0.013
Cronkite 1986,89	383	0.14	6.4	m	F	4.8	0.034
Cronkite 1986,89	383	0.14	6.4	m	F	17	0.012
Snyder 1988	320	0.2	2.6	m	M	26	0.018
Snyder 1988	320	0.2	2.5	m	M	27	0.019
Maltoni 1989	104	0.5	2.4	r	F	29	0.020

[a] Frac = fraction of lifetime exposed
[b] Sp = Species (m = mouse, r = rat)
[c] Assumes an intake of 10 m^3/day of contaminated air over 250 days/year and 45 years.
[d] Assumes 70 kg body weight and exposure over 250 days/year and 45 years.

Table 3. Cancer risk factors for benzene ingestion (derived from an animal study, NTP, 1986)

Risk factor characteristics					Risk factors for workers
Dose rate (mg/kg/d)	Fraction of lifetime exposed	Dose ($mgx10^7$)	Sp[a]	Sex	$(mg/kg/d)^{-1}$ [b]
50	0.7	3.4	r	M	0.0079
50	0.7	3.4	r	F	0.0095
25	0.7	2.7	m	F	0.021
50	0.7	1.7	m	M	0.020

[a] Sp = Species (m = mouse, r = rat)
[b] Assumes 70 kg body weight and exposure over 250 days/year and 45 years.

Dose rate/kg = 3.2 mg/m^3 x 10 m^3/d / 70 kg = 0.46 mg/kg/d

Fraction of lifetime exposed = 45 yr / 74 yr = 0.6

Select the risk factor from Table 1 which is based on exposure conditions most closely approximating those in this worker example. The exposure conditions of the Wong cohort more closely match those of the worker example than those of the Rinsky cohort. The highest risk factor will be used in this example, i.e. 35 x 10^{-4} $(mg/m^3)^{-1}$. Now theoretical lifetime excess risk can be calculated:

theoretical lifetime excess risk = 35 x 10^{-4} $(mg/m^3)^{-1}$ x 3.2 mg/m^3 = 0.01.

In addition to exposure at the PEL, it is of interest to consider air exposure levels at gasoline LUST sites as reported by Shamsky and Samimi (1987) and Kramer (1989). The mean exposure concentrations ranged from 0.1 to 6.7 ppm (8 hr-TWA) with an average value of 3.3 ppm (11 mg/m^3). Using the same risk factor as above, the theoretical lifetime excess risk is 0.04. The above risks are high and indicate that personal protection equipment should be worn by LUST site workers and workers exposed near the PEL.

To illustrate the use of an ingestion risk factor in a LUST exposure setting, assume soil concentration levels are in the range of 0.025 - 10 ppm and the soil intake

rate for workers to be 100 mg/d (Brown 1986). Table 4 shows the dose, dose rate/kg, fraction of lifetime exposed, and risks. The ingestion dose of LUST workers is

Table 4. Worker cancer risks from ingestion of benzene contaminated soil

Soil conc. (ppm)	Dose rate (mg/kg/d)	Frac[a]	Dose (mg)	Risk factor[b] $(mg/kg/d)^{-1}$	Theoretical lifetime excess risk
10	1.4×10^{-5}	0.6	11	0.021	3×10^{-7}
0.025	3.6×10^{-8}	0.6	0.03	0.021	8×10^{-10}

[a] Frac = fraction of lifetime exposed
[b] The risk factor of 0.021 was selected from Table 3.

several orders of magnitude less than those defining the ingestion risk factors in Table 3. Therefore, linear interpolation was used to calculate the risks shown in Table 4. For example, at 10 ppm:

Dose = $(10 \text{ mg}/10^6 \text{ mg}) \times 100 \text{ mg/d} \times 250 \text{ d/yr} \times 45 \text{ yr}$
= 11 mg

Dose rate/kg = $(10 \text{ mg}/10^6 \text{ mg}) \times 100 \text{ mg/d} / 70 \text{ kg}$

= 1.4×10^{-5} mg/kg/d

Fraction of lifetime exposed = 45 yr / 74 yr = 0.6

Risk = $0.021 \times 1.4 \times 10^{-5} = 3 \times 10^{-7}$

The theoretical lifetime excess cancer risk from the ingestion of soil at a LUST site is likely to be several orders of magnitude less than the inhalation risk.

The theoretical lifetime excess cancer risk from inhalation of benzene at the PEL is high. OSHA should consider significantly lowering the PEL for benzene and/or requiring the use of personal protection equipment. The theoretical lifetime excess cancer risk from inhalation of benzene at LUST sites is high, and the use of personal protection equipment is highly recommended. The theoretical lifetime excess cancer risk from ingestion of benzene at LUST sites is insignificant.

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry) (1989) Toxicological profile for benzene. PB89-209464

Brown HS (1986) A critical review of current approaches to determining how clean is clean at hazardous waste sites. Haz Waste Haz Mat 3:233-260

Cronkite EP, Drew RT, Inoue T, Bullis JE (1985) Benzene hematotoxicity and leukemogenesis. Amer J Ind Med 7:447-456

Cronkite EP (1986) Benzene: hematotoxixcity and leukemogenesis. Blood Cells 12:129-137

Cronkite EP, Drew RT, Inoue T, Hirabayashi Y, Bullis JE (1989) Hematotoxicity and carcinogenicity of inhaled benzene. Environ Health Perspect 82:97-108

Decoufle P, Blattner WA, Blair A (1983) Mortality among chemical workers exposed to benzene and other agents. Environ Res 30:16-25

Hallenbeck WH, Cunningham KM (1986) Quantitative risk assessment for environmental and occupational health. Lewis Publishers, Chelsea, MI

Kramer WA (1989) Benzene exposure assessment of underground storage tank contractors. Appl Ind Hyg 4:269-271

Maltoni C, Ciliberti A, Cotti G., Conti B, Belpoggi F (1989) Benzene, an experimental multipotential carcinogen: results of the long-term bioassays performed at the Bologna Institute of oncology. Environ Hlth Perspect 82:109-124

NTP (National Toxicology Program) (1986) Toxicology and carcinogenesis studies of benzene in F344/N rats and B6C3F1 mice. NTP TR 289.

Rinsky RA, Smith AB, Hornung R, Filloon TG, Young RJ, Olun AH, Landrigan PJ (1987) Benzene and leukemia:an epidemiologic risk assessment. New Eng J Med 316:1044-1050

Shamsky S, Samimi B (1987) Organic vapors at underground gasoline tank removal sites. Appl Ind Hyg 2:242-245

Snyder CA, Goldstein BD, Sellakumar AR, Bromberg I, Laskin S, Albert RE (1980) Inhalation toxicology of benzene:incidence of hematopoietic neoplasms and hematotoxicity in AKR/J and C57Bl/6J mice. Toxicol Appl Pharm 54:323-331

Synder CA, Sellakumar AR, James DJ, Albert RE (1988) The carcinogenicity of discontinuous inhaled benzene exposures in CD-1 and C57B1/6 mice. Arch Toxicol 62:331-335

Wong O (1987) An industry wide mortality study of chemical workers occupationally exposed to benzene. Brit J Ind Med 44: 365-395

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