

# Health risk assessment perspectives on chlorinated ethylenes: Focus on perchloroethylene toxicity values

Laura C. Green, Ph.D., DABT  
Edmund A.C. Crouch, Ph.D.

Cambridge Environmental Inc.  
58 Charles Street, Cambridge, MA, 02141



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58 Charles Street Cambridge, Massachusetts 02141

[www.CambridgeEnvironmental.com](http://www.CambridgeEnvironmental.com)

617-225-0810 FAX:617-225-0813

# Why focus on perchloroethylene?

- Commonly used solvent by dry cleaners
- Toxicity values imply it is a relatively potent carcinogen
- Combination of prevalent and toxic makes it a risk driver at many vapor intrusion sites



# Levels of Concern for Perchloroethylene

Benchmark	Concentration ( $\mu\text{g}/\text{m}^3$ )
NIOSH IDLH	1,020,000
ACGIH TLV	170,000
MA DEP Imminent Hazard	14



# Carcinogenicity (according to EPA)

- Perchloroethylene (draft, 2008)
  - Likely to be carcinogenic to humans
  - unit risk  $2 \times 10^{-6}$  to  $2 \times 10^{-5}$  m<sup>3</sup>/μg
- Vinyl chloride
  - Carcinogenic to humans
  - unit risk  $4 \times 10^{-6}$  m<sup>3</sup>/μg (adult) to  $9 \times 10^{-6}$  m<sup>3</sup>/μg (from birth)

# Perchloroethylene Unit Risk Factors

- US EPA (1985):  $4.8 \times 10^{-7} \text{ m}^3/\mu\text{g}$
- US EPA (1986):  $2.9 \times 10^{-7}$  to  $9.5 \times 10^{-7}$
- MA DEP (1990/95):  $5 \times 10^{-5}$
- OEHHA (1991):  $8 \times 10^{-6}$
- OEHHA (1992):  $5.9 \times 10^{-6}$
- OEHHA (2000): [ $\sim 2 \times 10^{-5}$ ; PHG]
- WHO (2006):  $5 \times 10^{-6}$  (direct extrap.)
- MA DEP (2007):  $1 \times 10^{-5}$
- US EPA (2008, draft):  $2 \times 10^{-5}$

# Implications (30 yr exposure; $\mu\text{g}/\text{m}^3$ )

	8 hr	24 hr
EPA 85	146	49
EPA 86	74	25
DEP90	1.4	0.5
OEHHA91	9	3
OEHHA92	12	4
OEHHA00	4	1.2
WHO06	14	5
DEP07	7	2
EPA08	4	1.2

# Implications (epidemiology)

## 20 yr exposure, lifetime risk

	3 ppm TWA	20 ppm TWA
EPA 85	0.0009	0.0062
EPA 86	0.0018	0.012
DEP90	0.10	0.65
OEHHA91	0.015	0.10
OEHHA92	0.011	0.076
OEHHA00	0.039	0.26
WHO06	0.0097	0.065
DEP07	0.019	0.13
EPA08	0.039	0.26

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# Why the differences?

- General agreement to use metabolized dose
- Animal data agrees with PBPK models
- Major metabolites similar animals/humans

BUT

- Rates of excretion differ substantially
- Long half-lives of metabolites in humans
- No radiolabel experiments in humans
- Depends how you calibrate your models

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# Fraction metabolized

Model	Inhalation	Oral
Bois et al., 1996	0.36	0.54
Ward et al., 1988	0.114	0.265
Reitz et al., 1996	0.077	0.179
Bois et al., 1990	0.069	0.142
Chen and Blancato, 1987	0.053	0.123
Gearhart et al., 1993	0.011	0.026

Source: Clewell et al. 2005

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- overall metabolism of tetrachloroethylene is relatively limited
- Several studies reported only about 1–3% ... inhaled were metabolized although ... as much as 20% or more ... may be metabolized over a longer period.
- E.g. Chiu et al. (2007) noted ... 0.4% of ... intake (1 ppm for 6 hrs)... in urine as TCA, total recovery ... only 82% ... imply 18% metabolized, but ... substantial uncertainty and variability ... consistent with previous studies at higher exposures. [EPA, 2008]

- Add uncertainties (factor of 2) gives range of order 1% to 70% used for setting values.
- Explains the principal differences between estimates through time
- Minor variations due to animal experiments selected, other evaluation methods applied (factor of 2 or so).



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# Where we are

- The values are out there and will undoubtedly get applied.
- NAS review process just beginning; project duration 15 months (original start date 6/1/06; actual 1st meeting about 11/13/08. “The report is expected to be issued in late 2009”).
- Then EPA has to respond.



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