2009 Risk Assessment Advice for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: January 11, 2010
Expiration Date: January 2015

Chemical Name:1,2,4-Trimethylbenzene

CAS: 95-63-6

Synonyms: Pseudocumene, Asymmetrical trimethylbenzene, psi-cumene

The database for 1,2,4-trimethylbenzene (TMB) consists of 2 short-term oral studies and 5 inhalation studies of varying durations. The currently available data for 1,2,4-trimethylbenzene (TMB) are insufficient to develop chemical specific health-based guidance for groundwater.

Health Risk Limits (HRLs) are available for a related trimethylbenzene, 1,3,5-TMB. 1,2,4-TMB and 1,3,5-TMB share similar chemical structures and similar metabolic pathways. A comparison of the available toxicity data for 1,2,4-TMB and 1,3,5-TMB suggests similar toxicity. The use of 1,3,5-TMB-based toxicity values to assess potential health risk from exposure to 1,2,4-TMB has been recommended by US EPA, NCEA (Superfund Program) and Cal EPA, OEHHA. The Minnesota Department of Health (MDH) recommends the use of the HRLs for 1,3,5-TMB to evaluate the potential health risks associated with exposure to 1,2,4-TMB.

The HRL values for 1,3,5-TMB are: Acute - Not Derived; Short-term, Subchronic and Chronic - 100 µg/L. For additional information on the derivation of HRL values for 1,3,5-TMB see: http://www.health.state.mn.us/divs/eh/risk/guidance/gw/trimethylbenzene135.pdf .

Volatile: Yes (highly volatile)

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No	Yes	No	Yes
Effects?	--	Unclear[1] (based on 1,3,5-trimethylbenzene)	Yes[2] (based on 1,2,4-trimethylbenzene & 1,3,5-trimethylbenzene)	--	Yes[3] (based on 1,2,4-trimethylbenzene)

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Not specifically tested. Increased white blood cell count with corresponding increases in neutrophil and lymphocytes were observed in one study that evaluated short-term oral exposure to 1,3,5-TMB (IITRI, 1995a) but this observation was not observed in an additional study conducted by the same investigators that also evaluated oral exposure to 1,3,5-TMB (IITRI, 1995b).

[2]Developmental toxicity was tested in one inhalation study that evaluated effects from exposure to both 1,2,4-trimethylbenzene and 1,3,5,-trimethylbenzene (Saillenfait, 2005). Effects include decrease in maternal body weight gain and food consumption, and reduction in fetal body weight.

[3]Neurotoxicity was tested only in inhalation studies resulting in behavioral changes in a 1,2,4-TMB study (Gralewicz et al, 1997 & 2000) and performance deficits in a study evaluating inhalation of white spirits known to contain 1,2,4-TMB (Lammers et al, 2007).

References (for 1,2, 4-TMB as well as 1,3,5-TMB):

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EPA National Center for Environmental Assessment http://cfpub.epa.gov/ncea/cfm/archive_whatsnew.cfm

EPA Office of Drinking Water http://www.epa.gov/waterscience/criteria/drinking/dwstandards.pdf

EPA Office of Pesticide Programs http://www.epa.gov/pesticides/reregistration/status.htm

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EPA Superfund Health Risk Technical Support Center. April 22, 2009. Provisional Peer-Reviewed Toxicity Values for 1,3,5-Trimethylbenzene (CASRN 108-67-8).

EPA Toxicity and Exposure Assessment for Children's Health (TEACH) http://www.epa.gov/teach/

EPA Voluntary Children's Chemical Evaluation Program (VCCEP)
http://www.epa.gov/oppt/vccep/pubs/chemmain.htm

European Union Pesticides Database
http://ec.europa.eu/food/plant/protection/evaluation/database_act_subs_en.htm

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World Health Organization: http://www.who.int/water_sanitation_health/dwq/gdwq3rev/en/index.html (search Chapter 8 Chemical Aspects and Chapter 12 Chemical Fact Sheets for chemical name)