# Carbon Disulfide Health Effects Assessment for HEAC discussion September 5th, 2008 (Revision of August 18, 2008)

## IDENTIFICATION

**Substance Name:** Carbon Disulfide

**CAS:** 75-15-0

**Synonyms:** CARBON BISULFIDE; CARBON SULFIDE; CARBON SULFIDE (CS2); CARBON SULPHIDE; DISULFURE DE CARBONE (DOT FRENCH); DISULFURO DE CARBONO (DOT SPANISH); DITHIOCARBONIC ANHYDRIDE; NCI-C04591; RCRA WASTE NUMBER P022; SULPHOCARBONIC ANHYDRIDE; SULPHURET OF CARBON; UN 1131; WEEVILTOX; BISULFURO DE CARBONO (DOT SPANISH); CARBON BISULPHIDE; CARBON DISULFIDE; CARBON DISULPHIDE

**Molecular Formula:** CS2

## CHEMICAL AND PHYSICAL PROPERTIES

**Physical state and appearance**: colorless to faintly yellow liquid

**Odor description:** Commercial - a sweetish aromatic; industrial - rotten cabbage or radish.

**Odor threshold:** 0.1-0.2 ppm (ACGIH, 1991)

**Molecular weight:** 76.14

**ppm to mg/m³** (at 25°C and 760 mmHg) 1 ppm = 3.11 mg/m3

**Vapor Pressure at 20°C:** 297 mm Hg

**Melting point:** -11.5°C

**Boiling point:** 46.5°C at 760 mm Hg

**Flammability:** Explosive limits: upper = 50%, lower = 1.25%

**Specific Gravity:** 1.293

## FORMS, USES, APPLICATIONS, and EXPOSURES

**Major Commercial Forms:** Grades of Purity: Commercial; technical; USP. Modern plants can manufacture the chemical to about 99.99% purity.

**Uses & Applications:** The most prominent industrial use of CS2 is in the production of viscose rayon fibers; it is also used in the production of carbon tetrachloride and cellophane. Carbon disulfide is used as a solvent for rubber, sulfur, oils, resins, and waxes, and has been used for soil fumigation and insect control in stored grain. Industrial processes that produce carbon disulfide as a by-product include coal blast furnaces and oil refining. EPA EPCRA database reports list five California oil refineries with reportable quantities of carbon disulfide.

**Exposure Routes:** inhalation, dermal, ingestion. One IH lab has reported taking air samples for CS2 but stopped after finding no significant exposures.

**Imports:** (1985) 1.36X10+9 g

**Exports:** (1985) 1.64X10+9 g

## MEASUREMENT INFORMATION:

**NIOSH Method:** NIOSH Method: 1600, Matrix: Air, Sampler: Solid sorbent plus drying tube (coconut shell charcoal, 100 mg/50 mg, and sodium, sulfate, 270 mg). Limit of Detection: 0.02 mg (one lab reported a 0.01 mg); Flow Rate: 0.01 to 0.2 l/min.; Estimated LOD for STEL sample is 2 ppm and TWA sample is 1.3 ppm (method sample volume max is 5 liters).

**Detector Tube**: Gastec detection limit: 0.3 ppm; Matheson-Kitagawa, detection limit 1 ppm.

**Biomonitoring:** It is metabolized to several metabolites including 2-thiothiazolidine-4-carboxylic acid (TTCA). ACGIH BEI: 5 mg TTCA in urine / gm creatinine.

## HUMAN HEALTH HAZARD DATA SUMMARY

### Chronic Toxicity:

Nervous system effects appear to be most sensitive target organ, reduced conduction velocity in the peripheral nerves and impaired performance in psychomotor testing. Other effects include alterations in serum lipids and blood pressure that are associated with increased risk of cardiovascular disease, systemic eye pathologies such as color vision and damage to the blood vessels of the retina, reproductive effects (developmental – reduced fetal weights), and with higher exposures increased mortality from heart disease. Carbon disulfide is listed under the State of California Proposition 65 as known to cause male and female reproductive toxicity and developmental toxicity. No evidence of carcinogenicity has been observed in limited epidemiological studies.

### Acute Toxicity:

CNS effects such as polyneuritis, psychosis, gastric disturbances, headaches, vertigo, impotence, tremors, sleep disturbances.

### Other Information:

Toxic amounts may be absorbed via the skin (Fairhill, 1957). One study calculated a human dermal absorption rate of 0.232 to 0.78 mg/cm(2)/hr (Dutkiewicz & Baranowska, 1967). Persons with disorders of the central nervous system, eyes, cardiovascular system, kidneys, and liver may be more sensitive to CS2 (Reprotext, 1999). Persons taking disulfiram (Antabuse) may be more sensitive to CS2 (Brugnone et al, 1992; Caroldi et al, 1994) since disulfiram is metabolized to CS2. Human subjects exposed for 6 hours to 10 ppm (30 mg/m³) CS2 exhibited an inhibition of oxidative N-demethylation (Mack *et al*., 1974). In persons using drugs such as analgesics, hypnotics, antidiabetics, and anticonvulsants, which are metabolized by oxidative N-demethylation, critical elevations in the plasma levels of these agents may be observed following exposure to CS2.

### Carcinogenicity:

ACGIH, A4, (ACGIH, 2005)

EPA, Not Assessed under the IRIS program, (IRIS, 2004)

IARC, Not Listed, (IARC, 2004)

MAK, Not Listed, (DFG, 2002)

NIOSH, Not Listed, (NIOSH, 2003)

NTP, Not Listed, (NTP, 2005)

## AGENCY and ORGANIZATIONAL SOURCES AND RECOMMENDATIONS:

**AIHA ERPG Values** (2006): ERPG-1: 1 ppm; ERPG-2: 50 ppm; ERPG-3: 500 ppm.

**ACGIH**: (2006) TLV-TWA 1 ppm, to protect from nervous system and all other organ systems effects, value based upon numerous references (not one in particular). Skin designation.

**ATSDR** (2000): 0.3 ppm for chronic (365 days and longer) inhalation exposures, this is a minimal risk level. ATSDR identified a LOAEL of 7.6 ppm from the study by Johnson et al. (1983), who found reduction in motor nerve conduction velocities in workers chronically exposed to carbon disulfide.  ATSDR adjusted for continuous exposure and applied uncertainty factors of 3 to derive a NOAEL and 10 for intraspecies variation.  To adjust this risk assessment for the workplace, the LOAEL to NOAEL factor of 3 was retained and the intraspecies factor was reduced to 3.  A cumulative uncertainty factor of 10 (two factors of 3 yields 10, as 3 is the approximation for the square root of 10) was applied to the worker LOAEL of 7.6 ppm to derive a recommended workplace exposure limit of 0.8 ppm.

**Cal/OSHA 5155, Table AC-1:** 4 ppm TWA, 12 ppm STEL, 30 ppm Ceiling, skin notation.

**U.S. EPA** (1995):  Inhalation RfC, 0.7 mg/m3. U.S. EPA (1995) derived an RfC of 0.7 mg/m3 for the critical effect of peripheral nervous system dysfunction.  A benchmark concentration for a 10% effect level of 17.7 ppm was derived from the Johnson et al. study in workers.  U.S. EPA adjusted for continuous exposure and applied an intraspecies uncertainty factor of 3, and an additional factor of 10 to “account for both database deficiencies, including concern for possible developmental effects at low levels, and to extrapolate to a lifetime exposure.” U.S. EPA provides no indication as to how the factor of 10 would be apportioned between database deficiencies and adjustment for lifetime exposure. Database deficiencies would still be relevant to workers, but adjustment for lifetime exposure would not; therefore it is recommended that this factor be reduced to 3. Dividing the BMC10 for workers of 17.7 ppm by an intraspecies factor of 3 and by an additional factor of 3 for database deficiency gives 2 ppm for an occupational exposure limit.

**Fed/OSHA:** 20 ppm PEL, 30 ppm Ceiling, maximum above ceiling 100 ppm for 30 minutes.

**National Institute for Occupational Safety and Health Recommended Exposure Limit:** (2005)1 ppm TWA; 10 ppm STEL, maximum above ceiling 100 ppm for 30 minutes; skin notation.

**National Research Council Emergency Exposure Guidance Levels, EEGLs** (1984): 10 minute: 200 ppm; 30 minute: 100 ppm; 60 minute: 50 ppm.

**OEHHA Acute Reference Exposure Level:** (1999)6 hour exposure (protective against severe adverse effects): 2.0 ppm (6.2 mg/m³). OEHHA (1999) derived an acute reference exposure level of 2 ppm for a 6 hour exposure to carbon disulfide to protect against reproductive/developmental toxicity and nervous system toxicity.  Based on the study of Saillenfait et al. (1989) a NOAEL of 200 ppm for significant reductions in fetal weight was identified.  A cumulative safety factor of 100 (10 for interspecies and 10 for intraspecies) was applied.

**OEHHA Chronic Reference Exposure Level:** (2001) 800 ug/m3 (300 ppb).  OEHHA derived a cREL for the critical effect of reduction in motor nerve conduction velocities.  A benchmark concentration for a 5% effect level of 6.86 ppm was derived based on the study of Johnson et al. (1983) in workers.  OEHHA adjusted for continuous exposure and applied an intraspecies uncertainty factor of 10.  Using the BMC05 of 6.86 ppm for workers and applying a reduced intraspecies factor of 3 gives a value of 2 ppm for an occupational exposure limit.

**OSHA:** (1989) proposed PEL, 4 ppm TWA and 12 ppm STEL, skin notation; based on cardiovascular disease, reproductive effects and neurological impairment. No one study was key but Johnson et al was cited.

**SUMMARY NOTE:** Johnson, et al was the key reference for recommendations described above of OEHHA cREL (2 ppm), US EPA RfC (2 ppm), ATSDR chronic inhalation (0.8 ppm). Johnson et al was also cited in the documentation of the ACGIH (1 ppm) and OSHA 1989 PEL rulemaking (4 ppm).

### More Recent Study:

One more recent study on neurological effects that was not referenced by the above entities. Godderis *et al.* (2006) studied viscose rayon workers exposed to carbon disulfide, with the purpose of evaluating exposure levels below the threshold limit value that was current at that time (31 mg/m3 or 10 ppm). The authors analyzed the data initially with the exposed group divided into < 31 mg/m3 (n = 60) and > 31 mg/m3 (n = 25) and compared those groups to a control group (n = 66). Neurobehavioral and clinical effects were assessed using various approaches including standardized and validated questionnaires, clinical neurological examination, computer-assisted neurobehavioral tests, and neurophysiological examinations (nerve conduction and electromyography [EMG]). When the authors determined that neurological effects were present at significant levels in the groups exposed both above and below 31 mg/m3, a further analysis of the results was conducted by grouping exposed workers into three categories: ≤ 10 mg/m3 (n = 34), >10 to ≤ 30 mg/m3 (n = 25) and > 30 mg/m3 (n = 26). In workers exposed at levels below 10 mg/m3 the following significant effects were observed relative to the control group: increased prevalence of positional tremor, increased prevalence of EMG abnormalities, increase in peripheral polyneuropathy, decrease in finger tapping (dominant and non-dominant hand), reduction in sural nerve SNAP (sensory nerve action potential) amplitude, reduction in sural nerve SCV (sensory conduction velocity), and reduction in sural nerve SSR (sympathetic skin response). Godderis *et al*. did not specify the range of exposures in the group exposed below 10 mg/m3. If 10 mg/m3 is taken as an approximate LOAEL for workers, one my derive a 1 ppm limit from an uncertainty factor of 3 (LOAEL to NOAEL).

## DRAFT HEAC RECOMMENDATIONS

**Permissible Exposure Limit: 1 ppm.** This recommended PEL is set to protect workers from decrements in peripheral motor nerve conduction velocities due to repeated and prolonged exposure to carbon disulfide. Studies in exposed workers and animals have identified the nervous system as a primary target for carbon disulfide.  Other health effects identified from occupational and/or toxicological studies include reproductive and developmental toxicity and cardiovascular disease.  Based on the existing risk assessments of ATSDR, U.S. EPA, and OEHHA, nervous system effects appear to be the most sensitive endpoint. These agencies based their recommended limits, 0.8, 2 and 2 ppm respectfully, on the study by Johnson et al. (1983). The more recent study by Godderis et al (2006) identified effects as low as 3 ppm, supporting an exposure limit as low as 1 ppm.

**Short Term Exposure Limit: no change to current STEL of 12 ppm.**

**Ceiling Limit: no change to current Ceiling limit of 30 ppm.**

**Other: Skin Absorption Notation**. This recommendation is based upon the work by Dutkiewicz and Baranowska (1967) who measured skin absorption in human volunteers. This study provides enough data to support a warning that skin absorption can be a significant route of workplace exposure. Other standard-setting agencies have indicated the risk of over-exposure via skin absorption (NIOSH, OSHA, ACGIH, FRG MAK and others).

## REFERENCES

* ACGIH (American Conference of Governmental Industrial Hygienists). Documentation of Threshold Limit Values and Biological Exposure Indices. Carbon Disulfide TLV Documentation, 2006.
* AIHA (American Industrial Hygiene Association). Emergency response planning guidelines. Akron (OH): AIHA; 1992.
* California Office of Environmental Health Hazards Effects (OEHHA) Acute Reference Exposure Level (REL) – Determination of Acute Reference Exposure Levels for Airborne Toxicants, Carbon Disulfide, March 1999.
* California Office of Environmental Health Hazards Effects (OEHHA) Chronic Toxicity Summary – Carbon Disulfide, November 14, 2001.
* Dutkiewicz T & Baranowska B: The significance of absorption of carbon disulfide through the skin in the evaluation of exposure, in: Brieger H & Teisinger J (Eds), Toxicology of Carbon Disulfide, Excerpta Medica, Amsterdam, The Netherlands, 1967, pp 50.
* Fairhill LT: Industrial Toxicology, Williams & Wilkins Company, Baltimore, MD, 1957.
* Godderis, L, et al. Neurobehavioral and Clinical Effects in Workers Exposed to CS2. Int J Hyg Environ Health, 2006, 209; 139-150.
* IRIS (Integrated Risk Information System). Inhalation Reference Concentration (RfC), US Environmental Protection Agency, Washington DC, 8/1/1995.
* Johnson BL, Boyd J, Burg JR, et al. Effects on the peripheral nervous system of workers’ exposure to carbon disulfide. Neurotoxicology, 4:53-66, 1983.
* National Institute for Occupational Safety and Health (NIOSH) Recommendations for a Carbon Disulfide Standard. DHHS (NIOSH) Publication No. 77-156, May 1977.
* National Institute for Occupational Safety and Health (NIOSH) Immediately Dangerous to Life or Health (IDLH) Documentation, printed from webpage on 11/16/2007.
* Occupational Safety and Health Administration (OSHA) Toxicologic Review of Selected Chemicals, Carbon Disulfide, remanded PEL documentation, January 19, 1989.
* Reinhardt F, et al, Electrophysiological Investigation of Central, Peripheral and Autonomic Nerve Function in Workers with Long-Term Low-Level Exposure to Carbon Disulphide in the Viscose Industry. Int Arch Occup Environ Health, 1997; 70(4): 249-56. (Abstract only)
* Toyama T & Sukurai H: Ten-year changes in exposure level and toxicological manifestations in carbon disulphide workers, in: Brieger H & Teisinger J (Eds), Excerpta Medica, Amsterdam, The Netherlands, 1967.
* Vanhoorne M, et al, Epidemiological study of eye irritation by hydrogen sulfide and/or carbon disulfide exposure in viscose rayon workers., Ann Occup Hyg, 1995, 39(3), 307-315.
* Warot P, Colleau P, & Meignie S: Arch Mal Prof 1964; 25:348.
* Wu L, et al; Study on DNA Damage of Germ Cells Induced by Carbon Disulfide Inhalation in Mice. Chinese Journal (unspecified), 21(7):833-834, 2005. (Abstract only)
* Xiaodong Tan, et al, Cross-sectional Study of Cardiovascular Effects of Carbon Disulfide Among Chinese Workers of a Viscose Factory. Int. J. Hyg. Environ. Health, 206 (2004); 217-225.