# Draft Carbon Disulfide (CS2) Health Effects Assessment Last Revised October 24th, 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. These effects were observed at higher exposures than those causing peripheral neuropathy. 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. For these effects to occur the exposure has to be 50 to 100 times exposures associated with peripheral neuropathy.

### 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** (1996): 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).

**Godderis et al (2006):**

A more recent study on neurological effects that was not referenced by the above agencies is Godderis *et al.* (2006). Viscose rayon workers in a plant operating since 1930 initially were divided into <10 ppm (EG1, n = 60) and >10 ppm (EG2, n = 25) exposure groups. Godderis based these groups on a cumulative exposure index calculated for each worker by multiplying the number of years in a job with the exposure and adding up these products. Godderis described the average yearly exposure to CS2 for the exposure groups as: EG1: 8.9 mg/M3 (+/- 1.1), and EG2: 59.2 mg/M3 (+/- 5.2). Also the cumulative exposure index was reported as: EG1: 59.5years\*mg/M3 and 746 years\*mg/M3. The exposure levels for the jobs were based upon recent and historic monitoring for homogeneous exposure groups (spinners, bleach, stable, and post-preparation). For historic exposure data Godderis (2006) references Vanhoorne et al. (1995 and 1991) describes exposures “for most jobs the average exposure to CS2 exceeds the present Threshold Limit Value (TLV) of 31 mg/M3.” Much of the sampling data was limited to two hour or less sample periods in jobs which admittedly have “highly variable exposures.” Regarding recent data Godderis refers to Bulat (2002) and states “from 1983 to 1992 CS2 concentrations ranged from 4 to 113 mg/M3. Since 1992, exposure dropped to levels remaining below TLV-values (max 32.4 mg/M3)”. The referenced papers do not clearly state what the exposure levels were at what year. Godderis references Bulat (2002) who states “it should be emphasized that the methods of analysis used in previous study differ from the methods used in the follow-up study. No drier tubers were used in series with the charcoal tubes in the first study. Having in mind that high humidity {admittedly present in the highest exposure workareas} can cause decreased adsorption of CS2 on active charcoal, we suppose that personal CS2 exposure in the previous study has been underestimated…”. Godderis (2006) does not discuss this or what exposure levels were applied to the years to develop the exposure groups. In this study Godderis (2006) assessed neurobehavioral and clinical effects using various approaches including standardized and validated questionnaires, clinical neurological examination, computer-assisted neurobehavioral tests, and neurophysiological examinations (nerve conduction and electromyography [EMG]). There was no mention of blinding the evaluators in any of these evaluations or tests. Of ten nerve conduction velocity tests, three where significant (see table of these below, geometric means of measurements):

| Nerve Conduction Velocity | Control Group | <10 ppm | >10 ppm | Unit |
| --- | --- | --- | --- | --- |
| Log (sural SNAP amplitude) | 10.50 | 5.58 | 2.86 | uV |
| Log (sural SCV) | 55.58 | 41.39 | 27.6 | m/s |
| Log (sural SNAP duration) | 1.93 | 3.43 | 5.29 | ms |

Godderis further divided the two exposure groups into three exposure groups: ≤3.3 (n = 34), 3.3 to ≤10 (n = 25) and >10 ppm (n = 26). Regarding the statistically significant nerve conduction findings Godderis states “Of the nerve conduction results, sural nerve SNAP amplitude and duration and sural nerve SCV were (borderline) significantly worse in all three subgroups…”. Because of the uncertainty in the exposure levels and borderline statistical significance, a conservative LOAEL would be 3.3 ppm. Applying an uncertainty factor of 3 (LOAEL to NOAEL), then a 1.1 ppm PEL is obtained.

## 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 borderline effects possibly as low as 3 ppm, therefore a 1 ppm exposure limit would likely prevent significant decrements in peripheral motor nerve conduction.

**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).

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