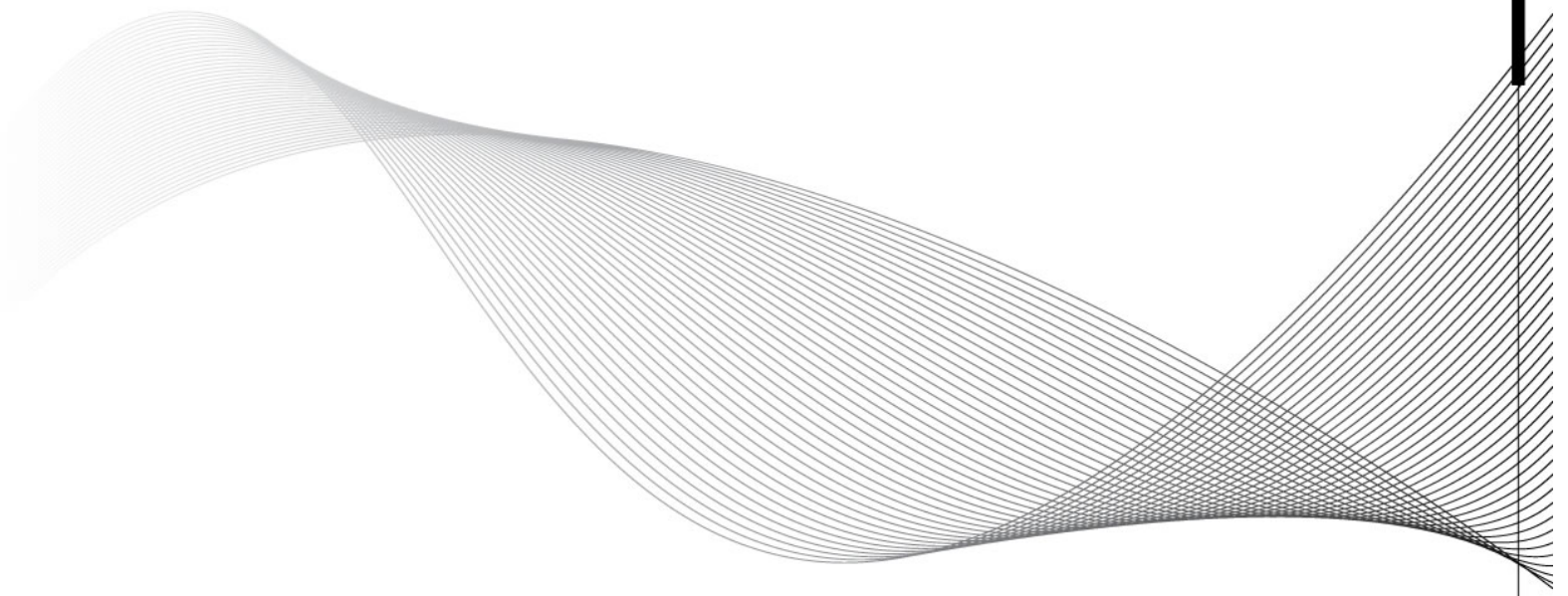
Social Europe



Recommendation from the Scientific Committee on Occupational Exposure Limits for chlorine

SCOEL/SUM/76

December 1998

European Commission

Table of Contents

Recommendation from the Scientific Committee on Occupational Exposure Limits for chlorine

8 hour TWA	:	-
STEL (15 mins)	:	0.5 ppm (1.5 mg/m^3)
Additional classification	:	-

Substance:

Chlorine Cl_2

Synonyms : Bertholite, molecular chlorine, dichlorine
EINECS N° : 231-959-5
EEC N° : 017-001-00-7
CAS N° : 7782-50-5
MWt : 70.91
Conversion factor (20°C, 101 kPa) : 2.95 mg/m^3 = 1 ppm
Classification : T; R23 Xi; R36/37/38

1. Occurrence/use

Chlorine is a dense greenish-yellow gas at ambient temperature and pressure. The odour threshold in most people is about 0.2 ppm (0.6 mg/m^3). It has a MPt of -101 °C, a BPt of -34 °C and a vapour pressure of 624 kPa at 20°C. The vapour density is 2.49 times that of air. It reacts with most organic and many inorganic compounds.

Chlorine is produced mainly by electrolysis of brine and is used widely in the manufacture of plastics, organic and inorganic chemicals, and as a disinfectant. It is also released when using sodium hypochlorite solution for bleaching, water treatment and disinfection. It is a very high volume chemical with a production rate in the EU in the order of several million tonnes per annum. Significant occupational exposure to chlorine is found mainly in the paper and pulp industry and at chlorine-manufacturing plants.

2. Health Significance

Following inhalation, chlorine is rapidly and almost completely transformed into hydrogen chloride and hypochlorous acid. It would be anticipated that the effects of inhaled chlorine would be predominantly local; chloride ions entering the circulatory system would be indistinguishable from dietary sources of chloride. No information is available on percutaneous absorption of chlorine, however in view of the reactions noted above, dermal uptake of chlorine is not of concern.

The acute toxicity of chlorine is high, with 1h LC50 values of 293-473 ppm (864-1395 mg/m^3) in rats and 137 ppm (404 mg/m^3) in mice (Zwart and Woutersen, 1988). The critical effects of chlorine are irritation of the eyes and upper respiratory tract. In a repeated inhalation study, rats were exposed to 0, 1, 3 or 9 ppm (0, 3, 9 or 27 mg/m^3) chlorine, for 6 h/d, 5 d/week for 6 weeks (Barrow *et al.,* 1979). Some deaths occurred at the highest exposure level, eye and upper respiratory tract irritation and slight degenerative changes in the liver and kidneys were observed at 3 ppm (9 mg/m^3), and at 1 ppm (3 mg/m^3) there were slight, occasional indications of irritation and inflammation in the upper and lower respiratory tract. In a well-conducted inhalation study in rhesus monkeys, exposure to 2.3 ppm (6.8 mg/m^3) chlorine for 6 h/d, 5 d/week for 1 year, resulted in eye irritation and mild focal hyperplasia and cilia loss in the nasal passages and trachea (Klonne *et al.,* 1987). The only finding at 0.5 and 0.1 ppm (1.5 and 0.3 mg/m^3) was "very mild" nasal epithelium hyperplasia in some of the treated animals, which was also observed in one of the control animals. The clinical relevance of this finding was questioned by the authors.

A recent study involved exposure of F344 rats and B6C3F1 mice to 0, 0.4, 1.0 or 2.5 ppm (0, 1.2, 3.0 or 7.4 mg/m^3) chlorine for up to 24 months (Wolf *et al.*, 1995). Female mice were found to be especially sensitive and were therefore exposed only 3 days a week. Various non-cancer-related lesions were observed in the nasal passages of both species at all exposure levels. The majority of these were also observed in control animals and were considered to represent exacerbation of background lesions normally seen in ageing rodents. The lesions were most severe in the anterior nasal cavity and included epithelial degeneration, hyperplasia and metaplasia. For many of the lesions there was a concentration-related increased in incidence and/or severity, with the effect being statistically significant at all concentrations studied. Rats were less sensitive than mice. There was no increase in the incidence of neoplasia in either species.

Ibanes *et al*. (1996) re-examined tissues from the studies of Klonne *et al.* (1987) and Wolf *et al*. (1995) in order to improve interspecies comparisons. At equivalent airborne

concentrations (about 2.5 ppm), chlorine-induced responses were less severe in rhesus monkeys, but extended more distally in the respiratory tract to involve the trachea, whilst treatment-related lesions were confined to the nose in rats and mice. Ibanes *et al*. (1996) concluded that respiratory tract airflow characteristics play a major role in lesion distribution and interspecies differences in severity. In this respect, the rhesus monkey is likely to be a better model for humans than rodents.

No mutagenicity or reproductive toxicology data are available.

In a volunteer study, exposure to chlorine at 1.0 ppm (3.0 mg/m^3) for 4 or 8 h, resulted in sensory irritation and transient impairment in lung function, whereas no effects were observed following exposure for 8 hours at 0.5 ppm (1.5 mg/m^3) (Rotman *et al.,* 1983). However, impairment of lung function is not considered to be a good indicator for irritation of the upper respiratory tract. D'Alessandro *et al*. (1996) exposed normal and hyperresponsive individuals to chlorine at 0.4 or 1.0 ppm (0.14 or 2.95 mg/m^3) for 60 mins. No significant changes were seen in the subjects exposed to 0.4 ppm (0.14 mg/m^3), who were all classified as hyperresponsive. At 1.0 ppm (2.95 mg/m^3), a significant fall in FEV_1 was recorded, which was greater in hyperresponsive individuals. At 24 hours after exposure, no significant deficits were seen. Further evidence that 0.5 ppm (1.5 mg/m^3) is a NOAEL in young healthy volunteers is provided by the study of Emmen and Hoogendijk (1997), in which 7 subjects were exposed to 0, 0.1, 0.3 and 0.5 ppm (0, 0.3, 0.9 and 1.5 mg/m^3) for 6 h per day on 3 consecutive days. No significant changes were observed in lung function parameters (forced vital capacity, forced expiratory volume in first second, maximal mid expiratory flow) or nasal lavage measurements (total cells, cell differentials, albumin, interleukin-8).

A number of epidemiological studies have been reported. An increased incidence of respiratory infections was noted in questionnaires completed by workers in a pulp mill (Ferris *et al.,* 1967, 1979). The exposure levels for chlorine were not adequately described and concomitant exposure to sulphur dioxide and chlorine dioxide occurred. Another study in pulp mill workers also indicated increased incidence of respiratory infections, with younger workers being more affected than older workers, possibly due to a healthy worker effect (Enarson *et al.,* 1984). Exposure was reported to be mainly to chlorine, with a mean 8h-TWA concentration of 0.18 ppm (0.52 mg/m^3). However, the information provided on the measurement data was insufficient to establish their validity and it is considered that the individual exposures were probably underestimated. These studies were therefore not considered to be adequate for use as a basis for proposing occupational exposure limits.

Recommendation

A constant exposure to 0.5 ppm (1.5 mg/m^3) has been shown to be without effect in two human studies, and also in rhesus monkeys, whereas there is clear evidence of irritation at 1.0 ppm (2.95 mg/m^3). On this basis, the SCOEL considered that occupational exposure levels should not exceed 0.5 ppm (1.5 mg/m^3), which is therefore proposed as a STEL (15 mins). Because the effects appear to be related to concentration in the air and not to duration of exposure, there is no requirement for an 8-hour TWA.

No "skin" notation was considered to be necessary.

At the levels recommended, no measurement difficulties are foreseen.

Key Bibliography

Barrow, C. S., Kociba, R. J., Rampy, L. W., Keyes, D. G. and Albee, R. R. (1979). An inhalation toxicity study of chlorine in Fischer 344 rats following 30 days of exposure. Toxicol. Appl. Pharmacol. 49, 77-88.

D'Alessandro, A., Kuschner, W., Wong, H., Boushey, H.A. and Blanc, P.D. (1996). Exaggerated responses to chlorine inhalation among persons with nonspecific airway hyperreactivity. Chest 109, 331-337.

Emmen, H.H. and Hoogendijk, E.M.G. (1997). Nasal inflammatory and respiratory parametres in human volunteers during and after repeated exposure to chlorine. TNO Report V97.517.

Enarson, D. A., Maclean, L., Dybuncio, A., Chan-Yeung, M. and Grzybowski, S. (1984). Respiratory health at a pulpmill in British Columbia. Arch. Environ. Health 39, 325-330.

Ferris, B. G., Burgess, W. A. and Worcester, J. (1967). Prevalence of chronic respiratory disease in a pulp mill and a paper mill in the United States. Br. J. Ind. Med. 24, 26-37.

Ferris, B. G., Puleo, S. and Chen, H. Y. (1979). Mortality and morbidity in a pulp mill and a paper mill in the United States: a ten-year follow-up. Br. J. Ind. Med. 36, 127-134.

Ibanes, J.D., Leininger, J.R., Jarabek, A.M., Harkema, J.R., Hotchkiss, J.A. and Morgan, K.T. (1996). Reexamination of respiratory tract responses in rats, mice and rhesus monkeys chronically exposed to inhaled chlorine. Inhalat. Toxicol. 8, 859-876.

Klonne, D. R., Ulrich, C. E., Riley, M. G., Hamm, T. E., Morgan, K. T. and Barrow, C. S. (1987). One year inhalation toxicity study of chlorine in rhesus monkeys (Macaca mulatta). Fund. Appl. Toxicol. 9, 557-582.

Rotman, H. H., Fliegelman, . J., Moore, T., Smith, R. G., Anglen, D. M., Kowalski, C. J. and Weg, J. G. (1983). Effects of low concentrations of chlorine on pulmonary function in humans. J. Appl. Physiol. 54, 1120-1124.

Rupp, H. and Henschler, D. (1967). Wirkungen geringer Chlor- und Bromkoncentrationen auf den Menschen. Int. Arch. Gewerbepath, Gewerbehyg. 23, 79-90.

Schmidt, A. and Jelnes, J. E. (1993). Occupational Exposure Limits: Criteria Document for Chlorine.

Wolf, D.C., Morgan, K.T., Gross, E.A., Barrow, C., Moss, O.R., James, R.A. and Popp, J.A. (1995) Two-year inhalation exposure of female and male B6C3F1 mice and F344 rats to chlorine gas induces lesions confined to the nose. Fund. Appl. Toxicol. 24, 111-131.

Zwart, A. and Woutersen, R. A. (1988). Acute inhalation toxicity of chlorine in rats and mice: Time-concentration-mortality relationships and effects on respiration. J. Hazard Mat. 19, 195-208.