Social Europe

Recommendation from the Scientific Committee on Occupational Exposure Limits for acrolein

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8 hour TWA:	0.02 ppm (0.05 mg/m3)
STEL (15 mins):	0.05 ppm (0.12 mg/m3)
Notation:	-

Substance:

Structural formula CH_2=CH-CHO
Molecular formula C_3H_4O

Synonyms Acrylic aldehyde; allyl aldehyde; acraldehyde; 2-propenal

EINECS N° 203-453-4

EEC N° 605-008-00-3

Classification: F; R 11 T +; R26 T; R25

CAS N° 107-02-8

MWt 56.06

Conversion factor (20°C, 101 kPa) 2.33 mg/m3 = 1 ppm

1 Occurrence/use

Acrolein is a colourless liquid with an acrid odour. It has a MPt of -87.7°C , a BPt of 52.7°C and a vapour pressure of 28.7 kPa at 20°C. It has a vapour density of 1.9 times that of air and is explosive in the range 2.8 - 31 % in air. The odour threshold is about 0.2 to 0.4 ppm (0.47 to 0.93 mg/m3).

Acrolein is used in the synthesis of other chemicals. such as acrylic acid derivatives, glycerol, methionine, glutaric aldehyde and a number of chemicals used in the surface treatment of textiles and paper. It occurs after combustion of organic materials such as plastics, glycerol-containing compounds, fats and cooking oils, wood and vegetation, gasoline and diesel. Acrolein is also present in cigarettes smoke. Acrolein is formed by reaction and photodecomposition of airborne pollutants, together with other aldehydes as formaldehyde.
The production rate in the EU is in excess of 20,000 tonnes per annum.

2 Health Significance

2.1 Toxicokinetics

Acrolein is well-absorbed by inhalation (Egle, 1972). Percutaneous absorption and skin irritation was demonstrated in rabbits but has not been investigated in humans. Acrolein reacts quickly at the site of contact with protein and non-protein sulfhydryl groups , especially with glutathione (Cassee et al. 1996). The predominant pathway for the metabolism is conjugation with glutathione and conversion to N-acetylcysteine compounds (IARC 1995). Acrolein is both a product and an initiator of lipid peroxidation (Kehrer .et al. 2000) and a metabolite of the chemotherapy drug cyclophosphamide (Hales, 1982).
There are no specific human data on toxicokinetics available.

2.2 Acute toxicity: Irritation

With continuous acrolein exposure (24 h/day), changes in body weight gain, serum biochemistry and
bronchial histopathology have been reported. Similarly, Cassee et al., (1996) reported higher labelling indices and histopathological changes in the nasal respiratory epithelium in rats exposed to 0.25 or 0.67 ppm (0.58 or 1.56 mg/m3) acrolein, 6 h/d for 3 days (LOAEL 0.57 mg/m^3). The RD_{50} for acrolein, causing a 50 % reduction in respiratory rate in mice amounted to 2.4- 6.6 mg/m^3 (ICPS 1992).
There is no clear indication for a sensitizing effect of acrolein in animals or in humans.

The critical effect of acrolein in humans is irritation of the eye and the respiratory tract. In healthy volunteers, exposure to 0.09 ppm (0.20 mg/m3) for 5 min is reported to cause slight irritation in the eyes, with 0.15 ppm (0.35 mg/m3) irritating the nose (Weber-Tschopp et al. 1977). In volunteers exposed to acrolein during 5 min the eye irritation score amounted to 0.471 (on a 0 to 2 scale) at 0.06 ppm (0.14 mg/m^3), 1.2 at 1.3 – 1.6 ppm and 1.5 at 2.0-2.3 ppm (Darley et al. 1960). The odour threshold was defined (Leonardos, 1969).at 0.21 ppm (0.48 mg/ m^3).

2.3 Repeated dose toxicity

A NOAEL of 0.06 ppm (0.15 mg/m3) was identified for the rat following 61 days continuous inhalation exposure (Gusev et al., 1966). Repeated exposure in rats has shown to result in impaired weight gain from 1.4 ppm (3.3 mg/m3) 6 h/d, 5 d/w for 13 weeks (Feron et al, 1978), with a NOAEL of 0.9 ppm (1.6 mg/m3). In a 6 weeks study in rats, guinea pigs, monkeys and dogs, exposed to 0.7 and 3.7 ppm lung effects were seen and the NOAEL is concluded to be < 1.6 mg/ m^3 (Lyon et al. 1970). Minor histological changes in the bronchial mucosa were seen in Dahl rats exposed to 0.4 ppm (0.9 mg/m3) acrolein for 6 h/d, 5 d/w for 12 to 13 weeks (Kutzman et al. 1984). Roemer et al (1993) examined the proliferative response in nasal, tracheal epithelial and free lung cells of rats exposed to 0, 0.2 or 0.6 ppm (0, 0.47 or 1.40 mg/m3) acrolein for 6 h/d on one or three successive days. After a single exposure, there was an increase in proliferation in all three cell types (visualised by 5-bromodeoxyuridine labelling) following exposure to 0.6 ppm (1.40 mg/m^3) acrolein, and in the trachea and lung at 0.2 ppm (0.47 mg/m3). The response was less marked after three repeated exposures. For long-term oral exposure studies (Parent et al. 1991,1992) found a NOAEL of 0.05 mg/kg bw) for rats and dogs and 2 mg/kg bw in mice.

2.4 Mutagenicity

Acrolein is a highly reactive substance and has been shown to give positive results in a number of *in vitro* genotoxicity assays. *In vivo* tests have given mostly negative results (IARC, 1995).

In the later EU-RAR final report (2001) acrolein is considered as a mutagen for bacteria and can induce gene mutations and sister chromatid exchanges, but no chromosomal aberrations in mammalian cells in vitro. These effect are restricted to a narrow dose range due to the high toxicity of acrolein in this test systems. Most of the in vivo tests are negative.

2.5 Carcinogenicity

Acrolein has been tested for carcinogenicity in rodents by administration in drinking water (Lijinsky and Reuber, 1987), inhalation (Feron and Kruysse, 1977), skin painting (Salaman and Roe, 1956), subcutaneous injection (Steiner *el al.,* 1943) and, most recently, by gavage (Parent el al., 1992a). All studies gave negative results apart from that one using acrolein in drinking water, which gave a marginal increase in the incidence of adrenal cortical tumours in female rats at the highest dose. Shortcomings have been noted (Parent el al., I 992a) on certain experimental aspects of this study which preclude interpretation of the findings.

There are no human data on cancerogenicity.

A recent IARC evaluation (IARC, 1995) concluded that there is inadequate evidence for the carcinogenicity of acrolein in experimental animals or in humans.

2.6 Reproduction toxicity

There was no evidence of teratogenicity in rats exposed to 0.55 ppm (1.3 mg/m3) acrolein (Bouley et al. 1976). A two generation gavage study of acrolein in rats provided no evidence of specific effects on reproduction (Parent et al., 1992b).

2.7 Effects of mixed aldehyde exposure

Exposure to mixtures of aldehydes are frequent both in the occupational situation as in the general environment. Apart from acrolein are involved formaldehyde, acetaldehyde and /or crotonaldehyde.
From studies in vitro and short-term inhalation studies on the irritation and nasal cytotoxicity, there seem not to be a greater hazard from the combined exposure to aldehydes in the same target organ and exerting the same type of effect (nasal irritation) then that associated with exposure to the individual chemicals (Cassee et al. 1996a). A competitive effect between the aldeydes for the same receptor was supposed. Other experiments have shown a competitive agonism between formaldehyde, acetaldehyde and acrolein in the decrease in breathing frequency in male rats (Kane et.al. 1978)

3 Recommendation

The main health effect of exposure to acrolein is irritation of the eyes, the mucosae and the skin, both in animals and in humans. The study of Roemer et al (1993), establishing a LOAEL of 0.2 ppm (0.47 mg/m3) for damage to the bronchial mucosa of rats was considered to be the best available basis for proposing an 8-hour TWA. An uncertainty factor of 10 was considered appropriate to allow for the absence of a NOAEL and of human data on prolonged exposure. The recommended 8-hour TWA is 0.02 ppm (0.05 mg/m3).
A STEL (15 min) of 0.05 ppm (0.12 mg/m3) is proposed to limit peaks of exposure which could result in irritation. This value is in line with the EU RAR conclusion (2001) and is based upon the human volunteer study of Weber-Tschopp et al (1977), indicating a LOAEL of 0.09 ppm (0.20 mg/m3) and the short- time exposure to acrolein vapours in volunteers of over 5 minutes for eye irritation (NOAEL of 0.06 ppm, 0.14 mg/m^3)(Darley et al. 1960) .
No "skin" notation was considered to be necessary.

At the levels recommended measurement difficulties are not foreseen with established methods (e.g. NIOSH 2501, UK MDHS 70) although further validation at lower concentrations may be required.

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