Pentacarbonyliron

(CAS reg no: 13463-40-6)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of pentacarbonyliron by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by MA Maclaine Pont, M.Sc. (Wageningen University, Wageningen, the Netherlands).

The evaluation of the toxicity of pentacarbonyliron has been based on the review by the American Conference of Governmental Industrial Hygienists (ACG99). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the data bases Toxline, Medline, and Chemical Abstracts, covering the periods of 1981 to July 1999, 1966 to November 1999, and 1937 to September 1999, respectively, and using the following key words: iron pentacarbonyl, iron carbonyl, carbonyls, iron, $Fe(CO)_5$, and 13463-40-6. The final literature search has been carried out in November 1999.

In July 2001, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	pentacarbonyliron
synonyms	:	iron pentacarbonyl; iron carbonyl
molecular formula:	:	$Fe(CO)_5$
CAS reg no	:	13463-40-6

Data from How 92.

Pentacarbonyliron is a viscous, colourless to yellow, oily liquid (ACG99).

3 Physical and chemical properties

molecular weight	:	195.9
melting point	:	-20°C
boiling point	:	103°C
flash point	:	-15°C (closed cup)
vapour pressure	:	at 20°C: 3.5 kPa
solubility in water	:	insoluble
log $P_{octanol/water}$	:	not found
conversion factors (20°C, 101.3 kPa)	:	1 mg/m^3 = 0.123 ppm 1 ppm = 8.15 mg/m^3

Data from ACG99, Che99, Lid96.

Pentacarbonyliron is a highly flammable, viscous, colourless to yellow, oily liquid. It is decomposed by light to iron monocarbonyl and carbon monoxide. It is pyrophoric in air and in an acetic acid solution; it burns to ferric oxide (ACG99).

The vapour is heavier than air and spreads over the floor, where it can be ignited from a distance. It reacts vigorously with oxidants, acids, and halogens (Che99).

4 Uses

Pentacarbonyliron has been used as an antiknock agent in gasoline in Europe. It may also be encountered in situations where finely divided iron comes into contact with carbon monoxide. It is a strong reducing agent (ACG99).

5 Biotransformation and kinetics

No data have been found.

6 Effects and mechanism of action

Human data

The committee did not find information on the health effects of exposure of humans to pentacarbonyliron

According to ACGIH, the clinical picture of acute exposure to high concentrations ot pentacarbonyliron is expected to resemble that of nickel carbonyl: immediate symptoms of headache and dizziness are followed within 12 to 36 hours by fever, cyanosis, cough, and dyspnoea; the primary effects are on the lungs, but degenerative central nervous system changes have been also reported (ACG99).

Animal data

acute toxicity data:

LC_{lo} inhalation 5.5 h rat	:	270 mg/m^3
LC_{lo} inhalation 45 min rabbit	:	2040 mg/m^3
LC_{50} inhalation 30 min rat	:	910 mg/m^3
LC_{50} inhalation 30 min mouse	:	2190 mg/m^3
LC_{50} inhalation 10 min mouse	:	7000 mg/m^3
LD_{50} intravenous rabbit	:	11 mg/kg
LD_{50} oral rabbit	:	12 mg/kg
LD_{50} oral guinea pig	:	22 mg/kg
LD_{50} dermal rabbit	:	240 mg/kg

Data from Lew92, Sun59.

Rats (Alderley park; n=4/sex/group) were exposed to pentacarbonyliron concentrations of 270, 122, and 57 mg/m^3 (33, 15, 7 ppm, resp), 5.5 hours/day, for 1, 2, and 18 days, respectively. In the high-concentration group, animals showed lethargy, respiratory difficulty, 4% COHb, and 3 animals were dead the next day. Histological examination revealed lung oedema and congestion. In the 15-ppm group, similar effects (mortality in 4 animals 3-4 days later, lethargy, respiratory difficulty, lung oedema and congestion) were observed. Exposure to 7 ppm did

not result in signs of toxicity or in macroscopic changes in lungs, liver, kidneys, spleen, and adrenals (no more data/details presented) (Gag70).

In a more recent study, rats (SPF-Wistar; n=5/sex/group) were exposed (whole body) to 81.5, 24, and 8.15 mg/m^3 (10, 3, 1 ppm, resp) pentacarbonyliron, 6 hours/day, 5 days/week, for 28 days. Because of severe toxicity (mortality) in the 10- and 3-ppm group, treatment was discontinued after 1 and 2 exposures, respectively. Two additional test groups were included and exposed to 2.4, and 0.82 mg/m^3 (0.3, 0.1 ppm, resp). In the 10-ppm group, animals showed abdominal respiration, piloerection, reddish crusts on the edges of the nose, deteriorated general state, and squatting posture. All animals were dead or sacrificed moribund by study day 4. Upon *postmortem* macroscopic and microscopic examination, there were minimal irritation of the upper respiratory tract (inflammatory changes in the submucosa of the nasal cavities and the trachea in 6/10 and 4/10 animals, resp), and effects on the lungs (intensive discolouration in 10/10, minimal to marked interstitial pneumonia in 10/10, minimal to marked regenerative proliferation in 8/10), spleen (strongly reduced size and lymphocyte depletion in 3/10 and 4/10, resp), mediastinal lymph nodes (2/5 females), and liver (yellowish, grey, or green-brown foci in 4/10). In the 3-ppm group, 50% of the animals were dead or sacrificed moribund by study day 4, showing signs similar to those seen in the 10-ppm group. In the surviving animals (2 males, 3 females), observed without further exposure for about 4 weeks, piloerection and accelerated respiration lasted up to study day 5 and 9, respectively. The absolute and relative lung weights of these animals were increased. *Postmortem* macroscopic and microscopic examinations revealed some minimal upper respiratory tract irritation (inflammatory changes in the submucosa of the nasal cavities and trachea in 1/10 and 3/10 animals, resp) and effects on the lungs (intensive discolouration in 5/10, minimal to marked interstitial pneumonia in 7/10, minimal to marked regenerative proliferation in 6/10), spleen (lymphocyte depletion in 2/5 females, resp) and liver (foci in 1/5 females). There were no effects on body weight development or on haematological, clinical chemical, and urinalysis parameters. In the animals exposed to 8.15 mg/m^3, 2.4 mg/m^3, and 0.82 mg/m^3 (1, 0.3, 0.1 ppm, resp), no substance-related clinical signs and findings or influence on body weight development were seen. There was a dose-related increase in carboxyhaemoglobin (COHb), measured after 17 days on test, which was statistically significant in male animals exposed to 1, 0.3, and 0.1 ppm and in female animals exposed to 1 and 0.3 ppm. The highest percentage of COHb was 2.1. Further, increases in absolute and relative lung weight were found (see Table

Tabel 1 Absolute and relative lung weights of rats (n=5/sex/group) exposed to pentacarbonyliron, 6 hours/day, 5 days/week, 28 days.

	males				females			
	0	0.82 (0.1)[a]	2.4 (0.3)	8.15 (1)	0	0.82 (0.1)	2.4 (0.3)	8.15 (1)
absolute lung wt (g)	1.1	1.2[b]	1.09	1.312[b]	0.96	0.93	0.94	0.94
relative lung wt (%)	0.29	0.31	0.29	0.336[b]	0.43	0.41	0.43	0.42

[a] concentrations in mg/m^3 and ppm (between brackets)
[b] $p \leq 0.05$

1). *Postmortem* macroscopic and microscopic examination did not reveal compound-related changes (Kli95).

In concordance with the Dutch Expert Committee on Occupational Standards (DECOS), another committee of the Health Council of the Netherlands (DEC92), the committee considers COHb levels ≤5% not to be toxicologically relevant, *i.e.*, there will be only a small or neglectible risk of effects on behaviour and mental capacities at these levels. Based on the relative lung weight effects in male animals, the committee concludes that the no-observed-adverse-effect level in this 28-day inhalation study is 2.4 mg/m^3 (0.3 ppm).

The committee did not find data on the potential mutagenicity/genotoxicity, carcinogenicity, and reproduction toxicity of pentacarbonyliron.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for pentacarbonyliron in the Netherlands is 0.08 mg/m^3 (0.01 ppm), 8-hour TWA, expressed as iron.

Existing occupational exposure limits for pentacarbonyliron in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

The committee did not find human data on effects of pentacarbonyliron but effects due to inhalation exposure to pentacarbonyliron may resemble those of nickel carbonyl, being effects on the lungs and the central nervous system in humans.

The committee did not find experimental animal data on the toxicokinetics or on the potential irritation and sensitisation of pentacarbonyliron.

Acute inhalation experiments in which 3 out of 4 (3/4) rats died following a 5.5-hour exposure to 270 mg/m^3 (33 ppm) and 4/4 rats following two 5.5-hour exposures to 122 mg/m^3 (15 ppm) showed pentacarbonyl to be a very toxic compound. Acute oral and dermal lethality data in rabbits (LD_{50}-values: 12 and 240 mg/kg bw, resp) demonstrated a similar potential following other routes.

In a 4-week inhalation study with intermittent exposure in rats (Kli95), exposure to 24 mg/m^3 (3 ppm) caused mortality in 50% of the animals, lung effects (increased absolute and relative lung weights, intensive discolouration, minimal to marked interstitial pneumonia, minimal to marked regenerative proliferation) in 50% or more of the animals, and occasional minimal upper respiratory tract irritation. At exposure to 8.15 mg/m^3 (1 ppm), there was only an increase in relative lung weights in male animals without accompanying histological changes while no effects were seen following exposure to 2.4 mg/m^3 (0.3 ppm).

The committee takes the NOAEL of 2.4 mg/m^3 of this study (Kli95) as a starting point in deriving a health-based recommended occupational exposure limit (HBROEL). For the extrapolation to a HBROEL, an overall assessment factor of 12 is established. This factor covers the following aspects: the type of effect, intra- and interspecies variation, and differences between experimental conditions and the exposure pattern of the worker. Thus, applying this factor - assuming that the dose inhaled by rats is equivalent to the dose inhaled by humans - and the preferred value approach, a health-based occupational exposure limit of 0.2 mg/m^3 is recommended for pentacarbonyliron, or of 0.05 mg/m^3, measured as Fe.

The committee recommends a health-based occupational exposure limit for pentacarbonyliron of 0.05 mg/m^3, measured as Fe, as an 8-hour time-weighted average (TWA).

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Annex

Occupational exposure limits for pentacarbonyliron in various countries.

country -organisation	occupational exposure limit[a]		time-weighted average	type of exposure limit	note[b]	lit ref[c]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	0.01	0.08	8 h	administrative		SZW01
Germany						
- AGS	0.1	0.8	8 h			TRG00
	0.2	0.8	15 min			
- DFG MAK-Kommission	0.1	0.81	8 h		[e]	DFG01
	0.2	1.62	30 min[d]			
Great Britain						
- HSE	0.01	0.08	8 h	OES		HSE01
Sweden	-	-				Arb00b
Denmark	0.1	0.8	8 h			Arb00a
USA						
- ACGIH	0.1	0.8	8 h	TLV		ACG01
	0.2	1.6	15 min	STEL		
- OSHA	-	-				ACG00
- NIOSH	0.1	0.8	10 h	REL		ACG00
	0.2	1.6	15 min	STEL		
European Union						
- SCOEL	-	-				CEC00

[a] Calculated as iron in all countries, except for Denmark
[b] S = skin notation; which means that skin absorption may contribute considerably to the body burden
[c] sens = substance can cause sensitisation
[d] Reference to the most recent official publication of occupational exposure limits
[e] Maximum frequency per shift: 4
[f] Listed among substances with MAK values but for which no pregnancy risk group classification could be made