Osmium tetraoxide

(CAS No: 20816-12-0)

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 osmium tetraoxide 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 KJ van den Berg, Ph.D. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of osmium tetraoxide has been based on the review by American Conference of Governmental Industrial Hygienists (ACG98). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the on-line databases Medline, Toxline, and Chemical Abstracts, covering the period 1966 to 26 April 1999 (19990426/UP), 1965 to 29 January 1999 (19990129/ED), and 1967 to 24 April 1999 (19990424/ED; vol. 130, iss. 18), respectively, and using the following key words: osmium oxide, osmium tetraoxide, osmium tetroxide, osmium IV oxide, tetraoxoosmium, and 20816-12-0. HSDB and RTECS, data bases available from CD-ROM, were consulted as well (NIO99, NLM99). The final literature search was carried out in April 1999.

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

2 Identity

name	:	osmium tetraoxide
synonyms	:	osmium tetroxide; osmic acid (anhydride); osmium oxide; perosmic acid anhydride; osmium IV oxide; tetraoxoosmium
molecular formula	:	OsO_4
structural formula	:	-
CAS number	:	20816-12-0

Data from ACG98, NLM99.

3 Physical and chemical properties

molecular weight	:	254.2
boiling point	:	130°C
melting point	:	39.5-41°C
flash point	:	not known
vapour pressure	:	at 27°C: 1.5 kPa
solubility in water	:	at 25°C: 6.23 g/100 mL
Log $P_{octanol/water}$	:	2.23 (estimated)
conversion factors	:	1 ppm = 11 mg/m^3
(20°C, 101.3 kPa)		1 mg/m^3 = 0.09 ppm

Data from ACG98, NLM99, Ric94, http://esc.syrres.com.

Osmium tetraoxide is a colourless to pale yellow solid with a disagreeable chlorine-like odour.

4 Uses

Osmium tetraoxide is mainly used as a biological stain for adipose tissues in histopathological laboratories. It is also applied in photography and as a catalyst in organic synthesis (ACG98, Ric94)

5 Biotransformation and kinetics

The committee did not find data on biotransformation and kinetics of osmium tetraoxide.

6 Effects and mechanism of action

Human data

In a very brief summary report, osmium tetraoxide in small (not further specified) amounts is reported to be irritating for the respiratory system and the eyes. In the eyes, moderate to severe conjunctivitis was observed, but also cases of blindness have been reported. Black discolourations of the skin may occur, caused by reduced osmium dioxide or metallic osmium. Also rashes on the face,

arms, and hands were observed. Prolonged inhalation of small amounts of osmium tetraoxide may lead to headache, insomnia, nausea, gastrointestinal complaints, diarrhoea, persisting irritation of the respiratory system with little secretion, and, under certain conditions, to pulmonitis. The highest concentration that could be tolerated for 6 hours without harmful effects was reported to be 0.001 mg/m^3 (Flu31). Because of lack of detailed information, the committee considers this report to be inadequate for use as a basis in standard setting.

Workers exposed to osmium tetraoxide have experienced irritation of the nose and throat that persisted for at least 12 hours after cessation of exposure (no data on concentration were given). Following a brief exposure to osmium tetraoxide vapour (concentration unknown), workers experienced delayed lachrymation and 'halo' effects (ACG98). At concentrations of osmium tetraoxide ranging from 0.1-0.6 mg/m^3, workers suffered from lachrymation and disturbances of vision, conjunctivitis, and complained of headache and cough. In most cases, recovery occurred within a few days (McL46).

In 2 cases of osmium tetraoxide poisoning in medical staff, altered respiratory functions indicative for a bronchitis with a tendency to chronicity were found (Vio69).

Osmium tetraoxide is considered a precipitating factor in the occurrence of occupational asthma (Whi88).

Osmium tetraoxide has been found corrosive to the skin and has produced dermatitis (ACG98).

Animal data

Irritation

Osmium tetraoxide as a 1 % solution, caused severe corneal damage, permanent opacity, and superficial vascularisation to a rabbit's eye (Bru33).

In rabbits (n=4) exposed to an initial calculated concentration of 1316 mg/m^3 for 30 minutes, pulmonary oedema was observed and deaths occurred after 4 days (Bru33).

The committee did not find data on the possible sensitising effects of osmium tetraoxide.

Acute toxicity

Acute 4-hour LC (less than 50% mortality) values for osmium tetraoxide of 40 ppm (400 mg/m^3) for rats and mice have been reported (ACG98).

An oral LD_{50} of 162 mg/kg bw has been reported for mice. Intraperitoneal LD_{50} values were 13.5 and 14.1 mg/kg bw for mice and rats, respectively (Ric94). These data were obtained from an unpublished report; the large differences between the LD_{50}s after oral and intraperitoneal administration cannot be explained.

Effects on the bone marrow have been reported after exposure of guinea pigs to osmium tetraoxide (concentration unknown) (ACG98).

No data from subacute, subchronic, chronic, or carcinogenicity studies were found.

Mutagenicity and genotoxicity

Osmium tetraoxide did not induce sex-linked lethals, visible mutations, or changes in fertility in *Drosophila* (Aue47).

Osmium tetraoxide was found to cause DNA damage as indicated by a positive result in the rec-assay system using recombination-proficient and -deficient strains of *B. subtilis* (Kad80, Kan80).

Biochemical studies indicate that osmium tetraoxide may bind to specific regions in the DNA double helix (Luk84), more specifically to thymidine-containing mismatches (Wur91), and may cause DNA damage by introduction of methoxyamine-binding sites and the formation of alkali-labile sites (Liu88).

Reproductive toxicity

In the chick embryo test, osmium tetraoxide had an LD_{50} of 1.2 mg/egg. No teratogenicity or abnormal developments were observed (Rid52).

The committee did not find other reproduction toxicity data.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for osmium tetraoxide in the Netherlands is 0.0002 ppm (0.002 mg/m^3), 8-hour TWA.

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

8 Assessment of health hazard

In humans, low (not specified) levels of osmium tetraoxide were irritating for the eyes, skin, nose, and respiratory system. At higher levels of exposure (not specified), it may be corrosive to the eyes and the skin, and also may cause systemic effects, pneumonia, and lethality. The highest concentration stated to be tolerated for 6 hours without harmful effects is 0.001 mg/m^3, but the relevance of this finding cannot be evaluated due to limited reporting.

No data on biotransformation and kinetics of osmium tetraoxide were found.

In experimental animals, osmium tetraoxide was corrosive to the eyes. No data on potential sensitising effects of osmium tetraoxide were found.

Acute 4-hour LC_{50} values of 40 ppm (400 mg/m^3) for osmium tetraoxide in rats and mice were reported. In rabbits, inhalation exposure to an initial concentration of 1316 mg/m^3 for 30 minutes caused pulmonary oedema and deaths after 4 days. An oral LD_{50} of 162 mg/kg bw for mice, and an intraperitoneal LD_{50} of 13.5 mg/kg bw for mice and of 14.1 mg/kg bw for rats have been reported. The large differences in LD_{50} values cannot be explained.

No data from subacute, subchronic, chronic, reproduction toxicity, or carcinogenicity studies were found.

Some evidence for a DNA damaging potential has been found in a *B. subtilis* system, but no data from other bacterial or mammalian cell mutagenicity or genotoxicity assay systems were found. Osmium tetraoxide is not mutagenic or genotoxic in *Drosophila.*

The committee considers the toxicological database on osmium tetraoxide is too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that there is insufficient information to comment on the level of the present MAC-value.

References

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Bru33 Brunot FR. The toxicity of osmium tetroxide (osmic acid). J Ind Hyg 1933; 15: 136-43.

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TRG00 TRGS 900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArbBl 2001; 2.

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Annex

Occupational exposure limits for osmium tetraoxide in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	0.0002	0.002	8 h	administrative		SZW02
Germany						
- AGS	-	-				TRG00
- DFG MAK-Kommission	-	-[c]				DFG02
Great Britain						
- HSE	0.0002	0.002	8 h	OES		HSE02
	0.0006	0.006	15 min			
Sweden	-	-				Arb00b
Denmark	0.0002	0.002	8 h			Arb00a
USA						
- ACGIH	0.0002	-	8 h	TLV		ACG02b
	0.0006	-	15 min	STEL		
- OSHA	-	0.002	8 h	PEL		ACG02a
- NIOSH	0.0002	0.002	10 h	REL		ACG02a
	0.0006	0.006	15 min	STEL		
European Union						
- SCOEL	-	-				CEC00

[a] S = skin notation, which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Listed among substances for which studies of the effects in man or in experimental animals have yielded insufficient information for the establishment of MAK values.