Social Europe

Recommendation from the Scientific Committee on Occupational Exposure Limits for Aerosols of Severely Refined Mineral Oils

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8 hour TWA	:	**5 mg/m³ (inhalable)**
STEL (15 mins)	:	**-**
Biological Limit Value	:	**-**
Additional classification	:	**-**

The main health concern with mineral oils (MO) is their carcinogenic activity (skin tumours) which is intimately related to their genotoxic polycyclic aromatic hydrocarbon (PAH) constituents. Depending on the degree of refining, different groups of MO can be delineated :

- *unrefined or mildly refined mineral oils*, which contain significant amounts of PAHs and are classified as Category 1 carcinogens in the EU,
- *severely refined mineral oils*, with negligible PAH content, which are considered non-carcinogenic in the EU,
- *other lubricant base oils with high PAH content* (>3% DMSO extractable fraction, note L of the 21st adaptation in the EC Directive on classification), which are classified Category 2 carcinogens in EU,
- *other lubricant base oils with low PAH content* (<3% dimethylsulfoxide (DMSO) extractable fraction), considered as non-carcinogenic as such. However, these products are used for the manufacture of metal working fluids (MWF) which may contain a large array of other chemicals either added for specific industrial applications (emulsifiers, biocides, corrosion inhibitors) or accumulated in the fluid during use through the solubilisation of metallic articles. Some of these contaminants are genotoxic and may contribute to a carcinogenic potential of MWF.

Unrefined or mildly refined MO and other lubricants base oils are, therefore, considered as non-threshold genotoxic carcinogens (SCOEL Category A; Bolt, H. M. *et al.* 2008) and the risk management for these substances should be based on the ALARA principle. An assessment of the health risk at low dose, assuming a non-threshold linear model might be performed if sufficient experimental and/or human data are available.

This SCOEL document covers non-carcinogenic severely refined mineral oils (SRMO) and is based on a DECOS publication on Aerosols of Mineral Oils complemented by a recent literature search conducted by SCOEL.

Substance Identity and Properties

MO are obtained by vacuum distillation of the residue from the atmospheric distillation of crude petroleum oils. Depending on differential volatility, several fractions are collected and further refined by solvent extraction, hydro-treatment and/or hydro-cracking. MO are liquids or solids and mainly consist of linear, branched and cyclic (naphtenic) saturated hydrocarbons with 15 or more carbon numbers as well as aromatics. Their and boiling is in the range 300-600°C, implying negligible vapour pressure under normal temperature conditions. They may also contain traces of organic sulphur, oxygen, nitrogen or metallic compounds. Aromatics can be removed by solvent extraction and by high-pressure hydrogenation (hydrocracking) to yield SRMO with less aromatics (<3% DMSO extractable

fraction). Hydrocracking also breaks long-chain into small alkanes and can also open naphtenic rings. SRMO include a range of substances with varying carbon numbers, names and properties (Table 1).

	EINECS	CAS number	Carbon number distribution
White mineral oils			
White mineral oil (petroleum)	232-455-8	8042-47-5	C15-C50
Light white mineral oil (petroleum)	295-550-3	92062-35-6	>C12
Severely hydrotreated oils			
Hydrotreated bright stock-based lubricating oil (petroleum)	276-735-8	72623-83-7	>C25
Hydrotreated bright stock-based lubricating oil (petroleum)	295-425-3	92045-44-8	>C50
Hydrotreated solvent-refined bright stock-based lubricating oil (petroleum)	295-426-9	92045-45-9	>C40

Table 1 : Severely refined mineral oils (SRMO).

1. Occurrence and Use

SRMO are mainly used as lubricants and aerosols may be generated in a number of industrial applications, including

- metal working,
- textile machinery,
- rock drills,
- mist lubrication,
- agricultural sprays,
- concrete mould release agents,
- corrosion prevention,
- printing inks,
- rubber extension,
- lubricant blending in open processes.

They are also used in food and pharmaceutical preparations.
Most of these industrial applications entail a potential for oil aerosol (mist) generation. In the 1990, the average occupational concentrations of these aerosols were in the range 1-2 mg/m³ (inhalable fraction) (reviewed in DECOS). Vapour exposure is less common in view of the low volatility of these compounds. Skin exposure is possible.

2. Health Significance

2.1 Toxicokinetics

Because of the complex and variable composition of compounds in this group, only a few factual data relating to their metabolism are available.

Animal studies with aerosols of SRMO indicate that absorption after inhalation is slow and limited, lung clearance being mediated by alveolar macrophages. The skin barrier is relatively permeable to hydrocarbons <C20. Gastrointestinal absorption of food-grade SRMO is limited to 1-5% and inversely proportional to the molecular weight of the constituents.

Clinical studies have indicated that inhaled SRMO are only slowly eliminated from the lung and can accumulate locally, possibly inducing lipid pneumonia. Macrophages can translocate a limited fraction of SRMO to the lymphatic system, the blood circulation, liver and fatty tissues.

The biotransformation of hydrocarbons in SRMO is generally very limited.

Unchanged hydrocarbons are excreted to a limited extent in feces and urine.

SRMO have low acute toxicity after oral, skin or inhalation exposure. Mild inflammatory lung reactions have been reported in mice after exposure to 200 mg/m³ (Wagner et al. 1961 cited in DECOS).

After excessive inhalation of SRMO aerosols, the main non-carcinogenic effects concern the airways and the lungs and are mediated by the interaction of parent hydrocarbon components with resident cells.

SRMO deposited in the lungs are taken up by macrophages (lipophages, foamy macrophages) and, presumably because of incomplete phagocytosis and or biotransformation, can induce an inflammatory reaction (exogenous[1] lipid or lipoid pneumonia, ELP) sometimes leading to a fibrotic response of the interstitial lung tissue. ELP is characterised by the focal accumulation of lipid-laden macrophages which progressively fill the alveoli (pneumonia). Giant multinucleated cell may develop within the alveolar organisation to form granulomas. Inflammation (mainly macrophages and lymphocytes) may invade interstitial tissues and possibly lead to the development of fibrosis. Lung function tests may reveal an obstructive, restrictive or mix syndrome, and a reduced diffusion capacity in most cases.

2.1.1. Animal data

In short-term and sub-chronic experimental studies, inhalation exposure to SRMO aerosols was generally associated with an accumulation of foamy macrophages and increased lung weight (reviewed in DECOS). Dalbey and Biles (2003, cited in DECOS) in their review of existing experimental data considered mild accumulation of alveolar macrophages in the absence of other toxicity not likely to constitute an adverse health effect and proposed an overall NOAEL of 50-150 mg/m³ for 13 weeks of exposure to MO. This assessment is essentially based on 2 studies:
Selgrade et al. (1990) exposed male and female rats to an oil fog of light-weight lubricating oil. Exposures were for 3.5 hours/day, 4days/week for 13 weeks at concentrations of 0, 200, 500 or 1500 mg/m³ with a particle size of approximately 1 micron (mass median aerodynamic diameter). Diffuse accumulation of macrophages in the alveoli was observed in all exposed groups. The degree of severity was concentration dependent. Histologic effects observed one day and 4 wk post exposure were similar and consistent with a persisting mild inflammatory edema. Minimal histopathologic changes and minimal increase in lavage fluid protein were the only effects observed at the 200 mg/m³ exposure level. There was a significant increase in lavage fluid protein, polymorphonuclear leukocytes and lung wet and dry weight following exposure to both 500 and 1500 mg/m³. At the highest exposure concentration, effects on lung weights were still evident 4 wk post exposure. Pulmonary function endpoints including total lung capacity, vital capacity, residual volume, diffusing capacity to CO, compliance, and end expiratory volume (EEV) were unaffected by oil fog exposure with the exception of EEV in males exposed at the 1500 mg/m³ level.
Dalbey (2001) exposed Sprague-Dawley rats during 6 hours/day, 5 days/week for 13 weeks to aerosol (particle size 1-2 µm) at concentrations of 0, approximately 50, 150, or 400-520 mg/m³ of 3 generic formulations mainly consisting of SRMO (cutting oil, generic gear oil, and generic commercial engine oil). The main observed effects were accumulation of foamy macrophages in pulmonary alveoli and alveolar walls, very mild thickening of alveolar walls due to foamy macrophages and a mixed cell infiltrate, and subtle epithelial hyperplasia. These histological changes were accompanied by concentration-related increases in wet lung weight and pulmonary hydroxyproline, whereas pulmonary function tests were generally unaffected. The overall NOAEL in this study was 50 mg/m³.

DECOS noted that, after 12-24 months exposure to a SRMO aerosol of 5 mg/m³, foamy macrophages with no other tissue response were detected in the lung and hilar lymph nodes of dogs, rats, mice and gerbils. Microgranulomas were found in the lungs of dogs and rats exposed to 100 mg/m³ of SRMO (DECOS).
This evaluation is derived from the study of Stula and Kwon (1978) in which dogs, rats, mice, and gerbils were exposed during 6 hours/day, 5 days/week, for periods up to 2 years, to an atmosphere containing a complex mineral oil-base aerosol (approximately 1 µm) at

[1] Endogenous lipid pneumonia is caused by the accumulation of cholesterol dropplets in the lungs, secondary to local tissue destruction.

concentrations of 5 or 100 mg/m³ (no intermediate doses were included). The study was designed to address a possible interaction of typical synthetic fiber adjuvants with MO in the textile industry. The test material contained 70% of paraffinic oil, the balance being adjuvants, including vegetable oils, sulphated vegetable oils, quaternary salts of alkyl phosphate esters, polyalylene waxes and resins. The test atmospheres also contained 1000 ppm acetone which is used as a fiber solvent. The results were compared with a previous study Wagner et al. (1964) in which animals were exposed to pure white mineral oil only (without adjuvants or acetone). Evidence of oil mist deposition (a few oil-laden lung macrophages) was detected in all species tested and at both concentrations. The development of oil microgranulomas was noted only at 100 mg/m³, in dogs and rats after 24 and 12 months of exposure respectively, but not in mice and gerbils, after 10-12 months of exposure. After a 10-month recovery period following 12 months of exposure, rats did not completely recover from the oil microgranuloma. The authors interpreted these lesions as similar to those observed with pure mineral oil Wagner et al. (1964).

No increased tumour incidence was observed in dogs and rats after long-term inhalation exposure up to 100 mg/m³ of SRMO. No tumours were observed after oral, derma, subcutaneous or intra-peritoneal exposure to SRMO. No genotoxic activity of SRMO was detected neither in bacterial nor in mammalian cell (mouse lymphoma, bone marrow cytogenetics, micronucleus) assays. Data on effects of SRMO on fertility and developmental toxicity are limited but did not evidence a concern for reprotoxicity (DECOS).

2.1.2 Human data

Exogenous lipid pneumonia is usually diagnosed in adults after prolonged and excessive oral or inhalation exposure to lipid-like products (Spickard, A., III et al. 1994). Similar lesions can be found in the liver and/or mesenteric lymph nodes after oral exposure. Most clinical cases of lipid pneumonia reported in the literature were caused by aspiration of MO in patients consuming paraffin-based laxatives, oil-based nose drops or pharyngeal injections of MO. In a retrospective study of 44 cases of ELP identified in France over the period 1992-93, 4 were associated with inhalation exposure to mineral oil products in occupational settings (Gondouin, A. et al. 1996). Cases of ELP have been reported after occupational exposure to oil spray (Penes, M. C. et al. 1990), motor oil spray (Vandenplas, O. et al. 1990), cutting oil (Perol, M. et al. 1989), low levels (< 5mg/m³) oil mist (Cullen, M. R. et al. 1981), paint aerosols (Abad, F. A. et al. 2003), rape seed oil (Kunze, P. 1985); but objective and quantitative data on exposure are often missing. Ameille et al. (1984) reported 4 cases of workers exposed to an aerosol of paraffin in a factory of cardboard cups, who developed typical ELP. One of these patients revealed progression to pulmonary fibrosis over 25-y after cessation of exposure Descatha, A. et al. (2006). Fire-eater pneumonia develops generally on an acute mode and is caused by the aspiration of volatile hydrocarbons (<C15) not MO.

SRMO are not or only slightly irritant and no sensitising potential has been reported.

Recommendations for scientifically-based occupational exposure limits

The respiratory system represents the critical organ of SRMO for setting an OEL. The occurrence of a few oil-filled macrophages in the lung of exposed animals, in the absence of any other toxicity, is considered as a physiological reaction. The accumulation of oil-laden macrophages (pneumonia), and certainly the formation of granuloma are,

however, adverse effects and these manifestations are considered as the critical health effect. The lowest NOAEL for inhalation exposure is 5 mg/m³ in a long-term experimental study in rats and dogs, a conservative value when compared to the NOAEL identified in the sub-chronic study (50 mg/m³). An OEL of 5 mg/m³ (inhalable) is recommended. This value applies exclusively to SRMO without additives and used only once (not recycled).

No short-term limit value is deemed necessary.

No skin notation is recommended.

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