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Linear Polydimethylsiloxanes (viscosity 10-100,000 centistokes) CAS No. 63148-62-9

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ECETOC

Joint Assessment of Commodity Chemicals No. 26

Linear Polydimethylsiloxanes

(viscosity 10-100,000 centistokes)

CAS No. 63148-62-9

September 1994

European Centre for Ecotoxicology
and Toxicology of Chemicals

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THE ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals.

In the programme, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

ECETOC is not alone in producing such reviews. There are a number of organisations that have produced and are continuing to write reviews with the aim of ensuring that toxicological knowledge and other information are evaluated. Thus a Producer, Government Official or Consumer can be informed on the up-to-date position with regard to safety, information and standards. Within ECETOC we do not aim to duplicate the activities of others. When it is considered that a review is needed every effort is made to discover whether an adequate review exists already; if this is the case the review is checked, its conclusions summarised and the literature published subsequent to the review assessed. To assist ourselves and others working in this field we publish annually a summary of international activities incorporating work planned, in hand, or completed on the review of safety data for commodity chemicals. Interested readers should refer to our Technical Report No. 30 entitled "Existing Chemicals: Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of commercial grade polydimethysiloxanes (CAS No. 63148-62-9) with variable viscosities greater than 10 centistokes. Purified polydimethylsiloxanes for special pharmaceutical applications are not included.

Linear Polydimethylsiloxanes
(viscosity 10-100,000 centistokes)
CAS No. 63148-62-9

CONTENTS

SECTION 1. SUMMARY AND CONCLUSIONS

Polydimethylsiloxanes (PDMS) belong to a group of polymeric organosilicon compounds which are commonly referred to as "silicones". This report covers PDMS fluids of viscosities 10 to 100,000 centistokes (cs). These are clear, colourless and odourless liquids that have non detectable vapour pressure and are insoluble in water. PDMS will strongly sorb to particulate matter in aquatic systems.

PDMS have a wide range of industrial and domestic applications especially as antifoaming agents, in personal care products, as textile treatment, polishing or release agents. The world wide production is estimated to be 150,000 tons a year.

Bulk amounts of PDMS waste from industrial use are predominantly recycled or incinerated. Used PDMS fluids contained in consumer waste and certain industrial waste streams are discharged diffusely and can be expected to enter waste water.

PDMS removal during wastewater treatment approaches 100% because of sorption onto sludge solids. Levels of PDMS in effluents range from non-detectable to ppb levels. Surface water levels of PDMS are generally below detection. Sewage sludge concentrations of up to several hundred ppm have been measured. Biodegradation on sludge solids during conventional aerobic and anaerobic treatment has not been observed. PDMS introduced into wastewater treatment systems will enter the environment as a component of sludge.

Sludge disposal include soil amendment, landfill, incineration and ocean disposal. PDMS introduced to the soil environment as a result of sludge amendment of soil is expected to abioticaly degrade to lower molecular siloxanols and possibly volatile oligomers. The breakdown products can bind to soil humic matter, can volatilise and can undergo photoinduced degradation or potentially biodegrade. The fate of PDMS in landfills has not been investigated but processes similar to those that occur in soil may also happen. PDMS combustion products include CO_2, H_2O, and amorphous silica.

PDMS will be sorbed to aquatic sediments as a result of small amounts discharged to surface waters from wastewater treatement plants or where ever waste water is discharged without treatment and where sludge ocean disposal is practiced. Sediment concentrations can range from trace levels to low ppm levels in areas of high industrial discharge. The fate of PDMS in sediments has not been fully investigated.

Bioconcentration of PDMS in aquatic organisms does not occur and bioaccumulation through the food chain in aquatic and terrestrial organisms has not been demonstrated.

No aquatic toxicity has been ascribed to PDMS.

PDMS of all viscosities display a very low acute toxicity via oral, dermal, inhalational, intraperitoneal, intradermal or subcutaneous routes of administration. Irritancy to the eye is low and no skin sensitising potential has been detected.

The potential routes of human exposure are by ingestion and dermal contact. PDMS are not absorbed through the skin, or from the gastrointestinal tract, from which it is rapidly excreted unchanged in the faeces.

Inhalation exposure normally does not occur due to the very low vapour pressure. Spray applications may give rise to the potential for aerosol exposure. The available toxicological data do not indicate any adverse effects.

Repeated dosage studies with PDMS of different viscosities demonstrated no significant adverse effects to a variety of mammalian species after oral, dermal or inhalative administration. In chronic studies, no adverse effects attributable to the treatment with PDMS were seen with rats, mice, dogs or monkeys.

In vitro genotoxicity studies with bacteria and mammalian cells provided no indications that PDMS have a mutagenic or clastogenic potential.

Limited studies with rats and rabbits displayed no clear evidence of a teratogenic effect of PDMS. Oral administration of PDMS to rats prior to mating had no effects on fertility, gestation, peri- and postnatal development. Long term dermal treatment of male monkeys with PDMS did not effect their reproductive performance.

No suppressive or stimulating influence of PDMS on the immune system has been demonstrated in studies on mice. In a study on man there was no evidence of dermal absorption of PDMS after repeated applications.

Overall, the available data indicate that PDMS do not present a health hazard for man. The safety of PDMS has been recognised by their widespread uses in many applications involving human exposure (e.g. food additives, personal care products) for more than 30 years.

SECTION 2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYSIS

Polydimethylsiloxanes (PDMS) are polymeric organosilicon substances with the structural formula shown below. The linear polymer is composed of dimethylsiloxy units with trimethylsilyl end groups. Polysiloxanes based on other units, with side groups other than methyl or with cyclic structures are not considered here. This report is limited to liquid PDMS with a viscosity of 10-100,000 centistokes (cs), corresponding to a mean molecular weight of approximately 1,300 - 74,000.

Commercially available PDMS are also referred to as:

- **'Siloxanes'**; general name for oligomeric or polymeric substances which are characterised by Si-O-Si bonds, methylgroups are usually bound to Si-atoms, but some siloxanes contain vinyl, hydroxyl or other groups in addition;

- **'Silicone Fluids'** or 'Silicone Oils', often abbreviated to **'Silicones'**; these terms cover all types of linear and branched siloxanes and the preparations and products made from them;

- **'Dimethicone'**; this is commonly used for PDMS in medical, pharmaceutical and cosmetic applications;

- **'E900'**; this is used for PDMS with a viscosity of 350-1,050 cs approved for specific applications as a food additive.

2.1 IDENTITY

Name: Polydimethylsiloxanes

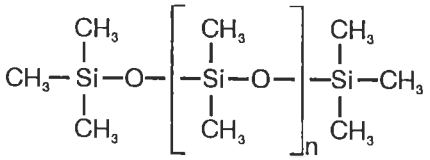
Abbreviation: PDMS

IUPAC Name: Poly[oxy(dimethylsilylene)]

CAS No: 63148-62-9

CAS Name: Siloxanes and Silicones, di-Me

Structural Formula:



Common Abbreviation: $MD_n M$

$M = (CH_3)_3 Si O_{1/2}$

$D = (CH_3)_2 Si O$

Molecular Weight: $162 + 74 \times n$ ($n \geq 15$)

The molecular weight, which determines the viscosity of PDMS, is governed by the number of $(CH_3)_2SiO$ units in the molecule. As with other polymeric substances, commercial PDMS contain a mixture of polymeric molecules exhibiting Gaussian molecular weight distribution. The following table shows the relationship between the viscosity, degree of polymerisation and molecular weight (Wacker, 1992)

2.2 PHYSICAL AND CHEMICAL PROPERTIES AND STABILITY

2.2.1 Physical Properties

PDMS are clear, colourless and odourless liquids with an extremely low vapour pressure. The physical properties vary only slightly with viscosity (degree of polymerisation). Some physical data are summarised in Table 2.

Table 1 **Relationship between viscosity, degree of polymerisation and molecular weight** (Wacker, 1992)

Viscosity (cs)	Average Number of D-Units	Number-Average Molecular Weights
10	15	1,300
50	40	3,000
100	70	5,000
1,000	200	15,000
10,000	500	37,000
100,000	1,000	74,000

Table 2 **Physical Data for PDMS**

Physical Form	liquid
Colour	colourless, clear
Viscosity (cs)	10 - 100,000
Density at 25°C ($g.cm^{-3}$)	0.93 - 0.98[1]
Vapour Pressure at room temp.	extremely low; not measurable
Boiling Point at 1013 hPa	decomposition at high temperature
Freezing Range (°C)	approx. -40 to -60
Specific Heat at 20°C ($J.g^{-1}°C^{-1}$)	1.45 - 1.55[1]
Refractive Index (n_D^{25})	1.398 -1.404[1]
Surface Tension at 20°C ($mN.m^{-1}$)	20 - 21[1]
Solubility ■ in water ■ in organic solvents e.g. hexane, toluene, chloroform, diethylether.	< 1 ppm miscible in all proportions

1 Silicone fluids AK, Company information - Wacker-Chemie München

Water Solubility

Trimethyl terminated siloxane molecules are extremely hydrophobic. Varaprath *et al* (1994) found that the water solubility of pure individual linear siloxanes decreases with increasing chain length, the solubility of octamethyltrisiloxane MDM, being 35 µg/l and that of dodecamethylpentasiloxane MD_3M, 0,07 µg/l.

Eales and Taylor (1983) found the solubility of PDMS (50 cs) in seawater to be 36 μg/l. PDMS spiked sediment was extracted with seawater at a flow rate of 10 ml/min.

Watanabe *et al* (1984a) eluted PDMS from coated glass beads by water (flow rate 3.5 ml/min). For various PDMS grades the water solubility was :

Mean MW 1,200	(ca.10 cs)	1,600 μg/l
Mean MW 6,000	(ca.100 cs)	560 μg/l
Mean MW 25,000	(ca.1,000 cs)	170 μg/l
Mean MW 56,000	(ca.10,000 cs)	76 μg/l

Parker and Tapscott (1993) reported the water solubility of PDMS 350 cs and 1,000 cs to be 201 μg/l and 90 μg/l respectively using the column elution method (EEC guideline 92/69, method A6, OECD guideline No 105).

The large differences in reported water solubilities can be attributed to the presence of low molecular weight materials and traces of hydroxy terminated siloxanes in commercial PDMS mixtures. Both the low molecular weight materials and hydroxy terminated siloxanes will have much greater water solubilities than the high molecular weight siloxanes. The measurable water solubilities reported by some investigators result from determining the total Si-content that is extracted from water with an organic solvent. Because extracted homologues are not characterised individually these extracts contain the more water soluble materials that are not representative of the MW distribution of the product. Therefore, actual PDMS water solubilities are probably in sub μg/l range as indicated by measurements of Varaprath *et al* (1994).

Octanol-Water partition coefficient

Measurements of octanol-water partition coefficients (P_{ow}) (following OECD guideline 107, shake flask method) were reported by Watanabe *et al* (1984a).

These findings are of questionable value because the commercial products examined contain variable portions of low molecular compounds and hydroxy terminated compounds resulting in a higher than expected water solubility value and, as a consequence, a log P_{ow} lower than expected. In addition, determination of PDMS concentrations in water is in general very difficult because of the special behaviour of these compounds in water.

PDMS	log P_{ow}
Mean MW 1,200	2.86
Mean MW 6,000	3.26
Mean MW 25,000	3.83
Mean MW 56,000	4.25

Using reverse phase High Performance Liquid Chromatography (HPLC) (similar to OECD guideline No 117) Bruggeman *et al* (1984) measured the "apparent" log P_{ow} of individual, fully methylated, linear siloxanes. For $MD_{14}M$(MW = 1,198) the apparent log P_{ow} was 12.5 which is unrealistically high. Log P_{ow} values of the most lipophilic monomeric organic chemicals normally do not exceed 7. The extremely high log P_{ow} value for PDMS is typical of log P_{ow} values for other polymers determined by HPLC methods. The high log P_{ow} values for polymers measured by HPLC result from long molecular chains and high molecular weights.

Adsorption and Desorption

The affinity of a substance to associate with soil and sediment in aquatic systems is described by the soil sorption coefficient K_d = [s]/[c], where [s] is the concentration on the solid and [c] is the concentration in water. The K_d per fraction of organic carbon in soil or sediment is K_{oc}. High K_d and K_{oc} values indicate strong sorption.

The K_{oc} of substances with well defined structures is straightforward to measure, but because PDMS is composed of molecules with similar structures but varying molecular weights, K_{oc} measurements are difficult to interpret. Watanabe *et al* (1985a) found a log K_{oc} of 3.69 for PDMS (10,000 cs). A commercial grade PDMS was used containing, most probably, small amounts of soluble siloxanols (hydroxy terminated siloxanes); the K_{oc} probably reflects the solubility of these siloxanols and has little bearing on the sorption of the hydrophobic PDMS. Measuring the sorption and desorption on sediments depends on the analytical methods, especially the methods to analyse PDMS sorbed to sediment. In the above study the recovery efficiency was not mentioned while in an earlier study Watanabe *et al* (1984b) reported a recovery efficiency of PDMS on sediment of 58%. This could suggest a similarly poor recovery in the above K_{oc}-study, resulting in a too low K_{oc}.

For pure octamethylcyclotetrasiloxane (a cyclic siloxane with MW = 296 consisting of dimethylsiloxy units) the measured log K_{oc} was 4.5 (Springborn, 1991). Large siloxane molecules such as occur in PDMS are expected to exhibit a similar or even higher K_{oc} value.

2.2.2 Chemical Properties and Stability

PDMS are chemically inactive substances with a remarkable stability to thermal and oxidative degradation and radiation. Dry heat of 150°C has little effect, but traces of formaldehyde can be detected (Wacker, 1994), resulting from reaction of oxygen with the methyl groups. Wet heat (steam) at 120°C or higher causes depolymerisation of PDMS. Strong acids and alkalis attack the Si-O-Si bonds, forming siloxane structures of varying molecular size (rearrangement); eventually a thermodynamic equilibrium of polymer species is established (Smith, 1991). Traces of catalyst residue from the manufacturing process may also cause rearrangement. Clay containing soils promote rearrangement and hydrolysis to form oligomers and water soluble fractions (See also 4.3.1).

PDMS do not absorb radiation energy over the spectral range of tropospheric light. High energy irradiation causes crosslinking reactions demonstrated by an increase in viscosity and resulting in a gel (Wacker, 1992).

2.3 ANALYTICAL METHODS

Analytical methods applicable to pure PDMS as defined in 2.1 have been reviewed by Crompton (1989), Smith (1991) and Kreshkov (1962).

Trace Analysis in Environmental Samples

Most PDMS determinations in environmental samples consist of a solvent extraction followed by a nonspecific Si analysis by either atomic absorption (AA) or inductively coupled plasma (ICP). Methods reported in the literature have used extraction solvents such as diethylether (Pellenbarg, 1979b), toluene (Tsuchitani *et al*, 1978), petroleum ether (Watanabe *et al*, 1984c), or hexane (Batley and Hayes, 1991). The extract is dried by anhydrous sodium sulphate and concentrated. The residue is dissolved in an appropriate solvent for the subsequent measurement of the Si-content by:

- AAS: Atomic Absorption Spectrometry (Tsuchitani *et al*, 1978; Pellenbarg, 1979b)
- ICP: Inductive Coupled Plasma Emission Spectometry (Watanabe *et al*, 1984c, Batley and Hayes, 1991).

In addition to the nonspecific methods of PDMS detection, Weschler (1981,1988) developed a specific pyrolysis-gas chromotography/mass spectrometry method for the analysis of PDMS. This method was developped to analyse PDMS associated to airborne particulate matter.

Comments

The reliability of PDMS analysis methods that appear in the literature vary as a function of extraction efficiency, ability to selectively extract PDMS, and method of detection. Recoveries of PDMS from water range from 69 to 100% (Section 5, table 5). Reported recoveries from sediment, soil and sludge are generally less than 74% (Section 5, tables 6 and 7).

Recently more efficient methods have been published. Lehmann (1993) used tetrahydrofuran to extract ^{14}C-PDMS (200 cs) from soil, applying a shaking method. Various soil types were spiked at 1, 10 and 100 mg/kg. Recovery efficiencies were > 90%. Recovery tests with sludge and sediment yielded efficiencies as high as in soil. For these extremely wet substrates an initial methanol extraction was recommended to remove water while leaving the majority (95%) of PDMS on the solid matrix. Harzdorf (1993) extracted PDMS (350 cs) from soil by soxhlet extraction (5 h) using diethylether or ethylacetate; after evaporation the solvent on a steambath the residue was dissolved in xylene and the silicon content determined by AAS. The recovery efficiency approached 100% with both solvents.

Analysis for PDMS in environmental samples using nonspecific methods of detection (AA and ICP) are also subject to positive interferences from inorganic silicates and other organo silicone compounds that may be coextracted with PDMS. Pellenbarg (1979b) and Siebert (1988) investigated the potential that clays minerals and silicates may be extracted with the same nonpolar solvents used to extract PDMS. Results from this work indicated that inorganic silica containing materials did not interfere with PDMS analyses. The potential interference from other organosilicone compounds has not been investigated.

Laboratory contamination is also a source of positive interference in the PDMS analysis. When handling environmental samples special care must be taken not to contaminate them with preparations containing PDMS widely used in laboratories (e.g. in hand creams, in lubricants for laboratory equipment and as release agents used during the manufacture of plastic containers). Frye (1987) pointed out that some published reports of PDMS in environmental samples could be artefacts resulting from contamination.

SECTION 3. PRODUCTION, STORAGE, TRANSPORT, USE

3.1 PRODUCTION

Commercial PDMS is produced by reaction of elementary silicon with methylchloride CH_3Cl in the presence of a copper catalyst. The resulting dimethyldichlorosilane $Si(CH_3)_2Cl_2$ is separated by distillation from by-products and transformed hydrolytically to linear OH-terminated siloxanes. Further polymerisation, controlled by the addition of an endcapping agent to replace the reactive OH-endgroup by trimethylsiloxy-groups $OSi(CH_3)_3$, produces the final polymer. More detailed information is given in the Ullmann's Encyclopedia (1993).

The total world-wide production of PDMS in 1993 is estimated by the ECETOC Task Force to be approximately 150,000 t/year.

3.2 STORAGE AND TRANSPORT

PDMS is not classified as "dangerous" under European and other chemical laws or under international transport regulations. Special packaging and labelling is not required. In Germany PDMS is classified in Wassergefährdungsklasse 1 (WGK 1) = slightly water polluting. In consequence it is necessary to comply with the regulations for the protection of ground water and surface waters.

3.3 USE

The viscosities of PDMS fluids mainly used are 350 cs and 1,000 cs, although other viscosities are used for specialised purposes. PDMS has a wide range of industrial and consumer uses, either in the pure form or as an ingredient of a formulated product (e.g. emulsions). The broad categories for use are:

Industrial applications with predominantly occupational exposure,

- Mold release agents,
- Lubricants (greases),
- Damping fluids,
- Hydraulic fluids,
- Heat transfer fluids,
- Liquid dielectrics (transformer cooling fluids),
- Industrial antifoams,

Industrial applications with potential for occupational and consumer exposure,

- Textile softening and water repellant agents,
- Softener in silicone rubber products (e.g. silicone sealants),

Industrial application with environmental exposure,

- Antifoams in waste water treatment plants,

Consumer applications,

- Polishes (for furniture and cars),
- Personal care products (hair care, skin care, soaps, cream, lotions),
- Cosmetics (lipstick, make-up, foundations),
- Antifoam in detergents,
- Domestic rinse agents,

Food applications,

- Antifoam in food processing eg beer, jam, etc.,
- Antifoam in frying fats and oils,
- Anticaking agent in powdered food.

SECTION 4. ENVIRONMENTAL DISTRIBUTION, BIOTRANSFORMATION AND ENVIRONMENTAL FATE

4.1 ENTRY INTO THE ENVIRONMENT

The presence of polysiloxanes in the environment is due exclusively to the activity of man. The release of PDMS to the environment during manufacture and transport is not significant (Howard *et al*, 1974). PDMS fluids have found a widespread use in industrial and domestic applications. Antifoaming agents, textile treatment agents, personal care products, polishing and release agents containing PDMS are discharged diffusely, mainly to waste water. Based on the use patterns the ECETOC Task Force estimates that approximately 50% of the PDMS fluids produced enters waste water. Howard *et al* (1974) also estimated that in the USA , half of the PDMS fluids is released to the environment after use.

The PDMS used in industrial applications such as transformer fluids, heat transfer fluids or damping fluids, is largely recycled or is incinerated. PDMS used as softener in silicone rubber products (e.g. silicone sealants) is expected to enter landfills when the rubber is discarded.

4.2 ENVIRONMENTAL DISTRIBUTION

Lane and Annelin (1983), reported by Buch *et al* (1984), used the "unit world model" of Neely and Mackay (1982) to calculate the equilibrium distribution of PDMS (MD_nM, n >5) in the environment using the water solubility, vapour pressure and the octanol/water partition coefficient (P_{ow}) in the model (Mackay calculation Level 1). The P_{ow} actually used was not reported. Because these physical data are uncertain (see 2.2.1) the results can be considered as indications only. The "unit world model" assumes that all necessary ways of transport required to reach equilibrium between the environmental compartments occur; this assumption is not necessarily correct for high molecular weight substances such as PDMS. The calculation suggests that 68.2% of PDMS will partition to terrestrial compartment, 31.6% to bottom sediment and 0.1% to suspended sediment. PDMS is not expected to be found in other environmental compartments (air, water, biota).

The transport of 84 mg hydroxy-endblocked polydimethyl siloxane (equivalent in physico chemical properties to PDMS 55 cs) from water to sediment was studied by Gettings and Lane (1982) in microcosms (9.6 l natural water, 2.4 l sediment). The substance spread on the surface of the water disappeared over a 6 week period, gradually forming tiny droplets in the water column which

eventually sorbed to suspended particulates and settled out becoming a component of the sediment (18.9 mg/g). Once in the sediment there was no evidence of its remobilisation. Very small amounts (42 µg/l) were found in the water at the end of the 24 week test. In another experiment, the same substance mixed with sediment prior to the test, remained immobile during a 16 week test period. In this case no extractable organosilicon could be detected in the water column (limit of detection 1 µg/l).

In waste water treatment plants (WWTP) PDMS is associated mainly with sludge (> 95%), minor amounts being sorbed to suspended particles in the effluent (Watts *et al*, 1993). In Europe, sludge is disposed of as landfill (44%), on agricultural land (37%), by incineration (9%) and by dumping at sea (7%) (Newman *et al*, 1989). Effluents are discharged to surface water; the suspended particles settle out and the PDMS will be found in the sediment.

Pellenbarg (1979a) reported that PDMS associated with WWTP sludge and the sludge dumped at sea do not migrate from the sediment. Movement of PDMS is expected only when sediment layers are moved e.g. by strong water currents.

The movement of PDMS in sediment was studied by Eales and Taylor (1983). North Sea sediment was spiked with 10,000 ppm PDMS (50 cs) and sandwiched by uncontaminated sediment in a tube. Seawater percolated through the layers for 30 days at a rate of 10 ml/min. Ninety-five% of the added PDMS remained in the sediment system. The authors conclude that PDMS is bound firmly to marine sediment and is unlikely to be remobilised by seawater.

No movement of ^{14}C-PDMS (200 cs) was detected in soil (Battelle, 1992a). Soil core microcosms (cores of sandy loam and silty clay) were planted with wheat and soy beans and studied for 7 months. The upper 20 cm of the 33 cm soil cores received single or multiple applications of ^{14}C-PDMS-containing sludge from a pilot-scale waste water treatment plant, resulting in PDMS concentrations of 0.22-6.56 mg/kg soil. The soil cores were watered regularly and the water leaching through them was collected. No radioactivity was detected in the leachate. At the end of the study the distribution of radioactivity in the cores was examined. Radioactivity was detected only in the upper 20 cm layer.

Thus PDMS fluids entering the environment are strongly sorbed to solid surfaces and are not expected to partition into the aqueous or atmospheric environment.

4.3 BIOTRANSFORMATION AND ENVIRONMENTAL FATE

4.3.1 Degradation in soil

Sewage sludge is the primary sink for PDMS (Section 4.2), and because sewage sludge is used as a soil amendment, soil is a significant environmental compartment for PDMS.

An early study found that soil clays caused rearrangement and hydrolysis of the polymeric siloxane bonds to yield volatile oligomers (mainly hexamethyldisiloxane and octamethylcyclo-tetrasiloxane) and water soluble siloxanols and silanols (Buch and Ingebrigtson, 1979). In dried soil spiked at 0.6% with 1,000 cs PDMS the half-life was reported to be approximately a month. Moisture contents of even only 1% caused inhibition of the reaction.

More recent studies using ^{14}C-labelled 200cs PDMS (at 100 mg/kg in a typical Michigan agricultural soil) showed PDMS breakdown within days as the soil dried from 12% water content to 3% (Lehmann *et al*, 1994a). The reaction was much slower when the soil was kept continually moist (12%). No cyclics were found, but numerous siloxanols were formed, and the ultimate degradation product was identified by GS-MS as dimethylsilanediol (Lehmann *et al*, 1994b). This molecule was lost from the soil by volatilisation and by biological oxidation to $^{14}CO_2$, while additional ^{14}C was covalently bonded to the humus (Lehmann *et al*, 1994b). Soil moistures and temperatures were typical of field conditions (Lehmann *et al*, 1994a), and these results imply that PDMS will degrade in soil and that any dimethylsilanediol formed from PDMS should biologically degrade, bind to the soil, or volatilise during the growing season. The volatilised silanols should demethylate by reacting with hydroxyl radicals in the atmosphere (Atkinson, 1991; Sommerlade *et al*, 1993) or in water (Anderson *et al*, 1987; Buch *et al*, 1984).

Siloxanols were also detected by HPLC-ICP analysis after PDMS had been spiked onto a dry standard soil matrix (Carpenter *et al*, 1994). Within 4-6 week of spiking, half of the PDMS had been converted to water soluble forms, consisting mostly of dimethylsilanediol. All of these results are consistent with earlier observations of PDMS in German soils, where Siebert (1988) found no difference in the organic Si levels of soils which had and had not received sewage sludge amendments. Since her calculations showed that repeated sludge applications, should have produced detectable differences in PDMS levels, she suggested that the degradation shown by Buch and Ingebrigtson (1979), and now confirmed by several recent studies, had been occurring.

Harzdorf (1993) spiked dried standard soil SP 31293 (Speyer/Germany) with 50 mg PDMS (350 cs) per kg and could extract about 100% PDMS immediately thereafter. After 10 day incubation only

48% and after 100 days 24% PDMS was extractable. During the incubation the generation of volatile siloxanes (octamethylcyclotetrasiloxane) was observed but not quantified.

In conclusion, there is evidence that in soil PDMS is degraded, e.g. in soils with < 3% moisture, often found in the surface layer of agriculture land.

4.3.2 Biodegradation

Biodegradation tests on PDMS with activated sludge bacteria have been conducted using conventional methods.

1.5 mg/l ^{14}C-PDMS (10 mg/l of a 15% PDMS (300 cs) emulsion) were incubated for 70 days with 10% sewage sludge in a 19 l reactor (Hobbs *et al*, 1975). ^{14}C-octadecane served as positive control. No $^{14}CO_2$, and no volatile organic degradation products were detected. All radioactivity was associated with particulate matter and no radioactivity was detected in the filtrate. Octadecane was extensively degraded under analogous conditions.

100 mg/l of PDMS (50 cs) emulsified by ultrasound was non-biodegradable by activated sludge (30 mg/l) over a test period of 30 days as measured by the biochemical oxygen demand (Street, 1980). At the end of the test period the bottle contents were extracted and 97% of PDMS initially added was recovered.

The biodegradability of various chemicals was studied in a laboratory size, continuously working sewage treatment facility (Matsui *et al*, 1975). "Silicone surfactants" (no detailed specification given but most probably a PDMS-antifoam emulsion was used) were found to be highly resistant to degradation.

The biodegradation of ^{14}C-PDMS (200 cs) has been studied in a laboratory-scale, waste water treatment plant under both aerobic and anaerobic conditions by monitoring the release of $^{14}CO_2$. The radioactive test substance (50 ppm) was added to aerobic sludge with and without acclimation to PDMS (28-35 days) prior to incubation and to anaerobic sludge with and without acclimation to PDMS (56-63 days) prior to incubation. In all cases the measured $^{14}CO_2$ was less than 0.1% of the added radioactivity. There was no detectable difference between acclimated and non-acclimated sludges. After termination of the tests an average of only 86% (74-92%) of the radioactivity could be detected by analysing the sludge, the supernatant and multiple Methyl Ethyl Ketone (MEK) rinsates of the test vessels. The major part of the recovered radioactivity was detected in sludge: 91-93% in aerobic sludge and 75-76% in anaerobic sludge (Battelle, 1992b).

^{14}C-PDMS (200 cs) loadings of up to 10,000 mg/kg activated sludge had no effects on the operating parameters of a pilot-scale waste water treatment facility with aerobic and anaerobic sludge digestion (Watts *et al*, 1993). After filtration of the effluent through a 0.45 μm filter all of the radioactive PDMS (>99%) was found in the sludge.

Ryan (1988) studied the fate and effects of PDMS (350 cs) in simulated residential septic tanks. No inhibition of the bacterial activity was observed; more than 90% of the PDMS added was recoverable by extraction and was shown unaltered.

Although activated sludge bacteria do not degrade PDMS, biodegradation has been found using special cultures of bacteria.

Bacteria from sludge of a biological WWTP from the chemical industry were cultured and enriched on polyether (Rast, 1993). The bacteria (gram negative, oxidase positive) were able to grow with octamethylcyclotetrasiloxane (D_4) as the only carbon source (D_4 is composed of 4 dimethylsiloxy-units, the same units as in PDMS). The test substance (50 μg/l) was eliminated within several hours. The degradation was shown to be oxygen dependent, degradation products could not be identified. Evaporation of D_4 was excluded.

Bacteria from soil of a silicone production plant in Czechoslovakia well acclimatised to PDMS by frequent spills were enriched by incubation with mineral medium and PDMS (Wasserbauer and Zadak, 1990). Strains growing on this medium were isolated for further degradation tests (*Pseudomonas putida*, *Pseudomonas fluorescens*) and then incubated with 1,000 ppm PDMS (15.6-4,875 cs) as the only carbon source for 12 days in the presence of a mineral medium. Degradation was followed by measuring the oxygen uptake in a respirometer and by the growth of the bacteria. Bacterial growth in the presence of a range of PDMS (15.6; 210; 350 and 475 cs) increased during the first 5 days and decreased thereafter. No reason was given for this decrease. With PDMS (1,485 and 4,875 cs) growth was observed during the 12 day observation period. The authors did not follow up the degradation by analysis of metabolites. The only indication of metabolism was the occurrence of Si-OH peaks in the IR-spectra of a CCl_4 extract.

In biphasic systems 200 g/l PDMS (20 cs) in water was not found to be degraded by microorganisms (*Pseudomonas sp.* and others) cultured for the degradation of xenobiotic substances such as chlorinated benzenes (Ascon-Carbera and Lebeault, 1993).

4.3.3 Aquatic fate

The water solubility of PDMS is extremely low. Under environmental conditions PDMS is resistant to hydrolysis. PDMS in waste water or WWTP effluents will sorb to solid particles which finally settle out.

Spills of PDMS fluids spread rapidly on water surfaces forming a film. Depending on the environmental conditions, PDMS films on water surfaces eventually forms tiny droplets in the water which sorb to suspended particulates and settle out (Gettings and Lane, 1982).

Spills of PDMS fluids on natural waters are not expected to pose a risk of oxygen depletion in water because the permeability of oxygen in PDMS is high (Clark and Gollan, 1966). Goldfish survived for several weeks while being completely immersed in PDMS of low viscosity.

Watanabe *et al* (1986) and Nagase *et al* (1988) expressed their concern that PDMS found in sediment may react with inorganic mercury to form toxic methyl mercury derivatives, since PDMS reacts at 80°C with mercurychloride to form small amounts of methyl mercury. Frye and Chu (1988) demonstrated that it is highly improbable that methyl mercury is formed under environmental conditions. Even when using watersoluble organosilicon compounds like trimethylsilanol and dimethylsilanediol to guarantee intimate contacts no methyl mercury was formed in the presence of mercuric chloride ($HgCl_2$).

In conclusion, in the aquatic environment PDMS fluids have not been shown to undergo degradation. They are eliminated by partitioning to sediment.

4.3.4 Terrestrial fate

The patterns of use and disposal routes suggest that PDMS will be present in soil only as result of applications of sewage sludge. Although no biodegradation of PDMS has been reported in sewage sludge, in a soil environment PDMS is expected to undergo abiotic degradation (see Section 4.3.1).

An increasing proportion of sewage sludge is now incinerated. At temperatures of > 800°C PDMS bound to sewage sludge is combusted to form CO_2, H_2O and amorphous silica (Lipowitz and Ziemelis, 1976). CO_2 and H_2O are discharged with the exhaust gases, while silica either becomes trapped in the ash or in the exhaust filter. In both cases the disposal route for amorphous silica is landfill. However, under the operating conditions of a waste incineration plant (conditions not reported) Watanabe *et al* (1985b) found small amounts of unburnt PDMS in the ash.

Landfill is the major disposal route for PDMS bound to sewage sludge (Newman *et al*, 1989). The very low water solubility, and findings in soil leaching studies show that PDMS will remain in the landfill bound to particulates. No published references are available on the presence of PDMS in landfill leachate, despite extensive monitoring programmes for evaluating ground-water pollution from municipal landfill sites. Under acidic or alkaline landfill conditions PDMS molecules may be cleaved forming siloxanes with lower molecular weight (see 2.2.2). If in the landfill clay containing minerals are present a degradation as reported in soil can be assumed (see 4.3.1).

4.3.5 Summary of fate

Large volumes of PDMS fluids from industrial use are predominantly recycled or incinerated. PDMS fluids contained in consumer waste and certain industrial waste streams will enter waste water. PDMS is not biodegradable in activated sewage sludge and leaves WWTP mainly sorbed to sludge. Where effluent discharge is not via a WWTP, PDMS will enter surface water, predominantly bound to particulate matter. In surface water the suspended particles will settle out with the PDMS entering the bottom sediment.

In sewage sludge deposited on landfills, biological degradation of PDMS is not expected. Depending on the chemical composition of the landfill chemical degradation may occur. When dumped at sea the sludge will sink to the bottom becoming part of the bottom sediment in which degradation is not known. When incinerated, PDMS in sludge is combusted to CO_2, H_2O and amorphous silica (SiO_2). PDMS in sludge applied to agricultural land has been shown to be degraded abiotically (see diagram below).

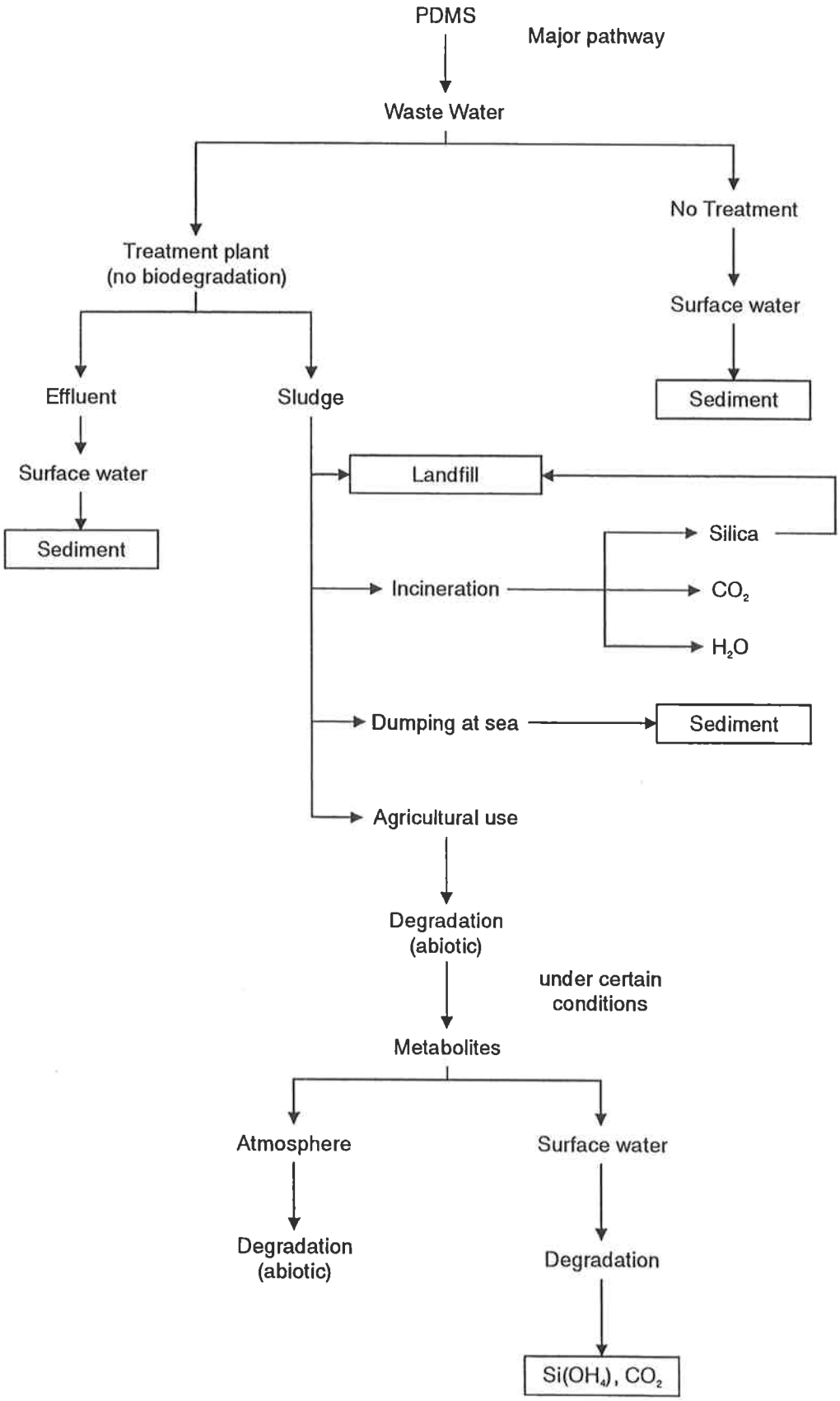
4.4 BIOCONCENTRATION AND BIOACCUMULATION

4.4.1 General consideration

Bioconcentration is the uptake and the accumulation of a chemical by a living organism from the surrounding medium, usually water. Bioaccumulation (biomagnification) is the uptake and accumulation of a chemical through the food chain.

For many organic substances, a relationship has been established between the n-octanol/water partition coefficient (P_{ow}) and the bioconcentration factor in fish (BCF, the ratio of chemical concentration in fish to that in water) (Neely *et al*, 1974 ; Veith *et al*, 1979). This relationship however, is not valid for substances of molecular weight greater than 600 since they do not pass readily through cell membranes (Zitko *et al*, 1976; Opperhuizen *et al*, 1985; Ankiler *et al*, 1988).

Figure 1 Pathways and Fate of Polydimethylsiloxanes



Because PDMS has a mean molecular weight of more than 1,300 the relationship between log P_{ow} and log BCF as proposed by the Neely *et al* (1974) and Veith *et al* (1979) cannot be applied.

4.4.2 Bioconcentration

Annelin and Frye (1989) studied the uptake by fish of low molecular weight, individual, fully methylated linear siloxanes (MD_2M to MD_7M). Those of molecular weight ≥ 384 (MD_3M) were not taken up by the fish after an exposure of ≥ 35d. Exposure concentrations were 2-300 µg/l. The detection limit in whole fish (rinsed with acetone) was 300 µg/kg and in water 1 µg/l. This study demonstrates that PDMS-molecules with MW > 1,300 can not bioconcentrate in fish.

Hobbs *et al* (1975) studied the bioconcentration of an emulsion containing 15 % ^{14}C-labelled PDMS (300 cs) with *Lepomis macrochirus* (Bluegill sunfish). These were exposed for 30 days in static conditions to controlled concentrations of PDMS. At the highest concentration studied, 1.5 mg/l PDMS, the amount of radioactivity detected in muscle remained low and after the 14th day, despite slight fluctuations, a steady state was reached and the BCF remained less than 1.

Opperhuizen *et al* (1987) studied the bioconcentration of PDMS (5 cs) containing a mixture of various MD_nM (n = 3-17) in *Poecilia reticulata* (guppies) which were exposed over a 20 day period in a tank with circulating water saturated with the test substances. For PDMS (Md_nM, n ≥ 15) as defined in 2.1 no uptake was observed.

After a 8 days exposure in water containing 70 mg/l emulsified PDMS (50 cs), the bioconcentration factor in plankton and annelids was very low (Aubert *et al*, 1985 ; Guillemaut *et al*, 1987).

The results of bioconcentration studies with PDMS are summarised in table 3.

The results show that the bioconcentration of PDMS in fresh water and marine species is very low. The increase of BCF with increasing molecular weights as reported by Watanabe *et al* (1984a) are in contradiction to all other results. This could be related to the strong adsorption properties of PDMS to surfaces, even to the skin of fish. Watanabe *et al* did not indicate whether the fish was cleaned prior to analysis and whether whole fish or muscle meat was analysed.

4.4.3 Bioaccumulation

The results of bioaccumulation studies are summarised in table 4.

Table 3 Bioconcentration in Water Organisms

PRODUCT	ORGANISM	EXPERIMENTAL CONCENTRATIONS (mg/l)	BCF[1]	REFERENCE
^{14}C-PDMS 300 cs 15 % emulsion	*Lepomis macrochirus*	1.5	0.16 to 0.5 after the 14th day	Hobbs *et al*, 1975
$MD_{15}M$ $MD_{16}M$ $MD_{17}M$	*Poecilia reticulata*	saturation	< 10 < 10 < 10	Opperhuizen *et al*, 1987
Commercial PDMS MW: 1,200 6,000 25,000 56,000	*Carp sp.*	Saturated solutions measured concentrations 1.330 0.486 0.135 0.060	 2.9 7.1 386 1,250	Watanabe *et al*, 1984a
PDMS 50 cs 35 % **emulsion**	Phytoplankton (*Tetraselmis sp.*) Plankton (*Tetraselmis sp.* and *Artemia salina*) Annelid (*Nereis diversicolor*)	70	2.08 1.9 0.036	Aubert *et al*, 1985; Guillemaut *et al*, 1987

1 BCF: Bioconcentration Factor

Annelin (1979) found no significant bioaccumulation of a PDMS (50 cs) fluid in *Ictalurus melas* (bullhead fish). A group of 64 fish was fed daily with food spiked with PDMS during 10 days. The daily total amount of PDMS eaten by the group was approximately 1g.

Opperhuizen *et al* (1987) fed *Poecilia reticulata* (guppies) with food spiked with PDMS (5 cs) containing some high molecular weight siloxanes ($MD_{15}M$, $MD_{16}M$, $MD_{17}M$). The concentration of these siloxanes was approximately 30 mg/kg food (32 mg/kg food for $MD_{17}M$). After 12 week of exposure siloxanes MD_nM with $n \geq 13$ were not detected in the whole fish.

Aubert *et al* (1985) and Guillemaut *et al* (1987) studied the biomagnification of a PDMS emulsion in four food chains in the marine environment. Organisms in the first level of the food chain were exposed to 70 mg PDMS (50 cs)/l emulsified in water; the concentration in them was measured (see table 4). However, whether this represents the maximum attainable concentration, is not known. The organisms were subsequently fed to organisms of a higher level in the food chain; they were kept together in water containing the same concentration of PDMS under static conditions.

Table 4 Bioaccumulation in Organisms Fed with Contaminated Food

PRODUCT	ORGANISM	EXPERIMENTAL CONDITIONS	BIOACCUMULATION FACTOR	REFERENCE
PDMS (50cs)	*Ictalurus melas*	exposure from food	< detection level	Annelin, 1979
$MD_{15}M$ $MD_{16}M$ $MD_{17}M$	*Poecilia reticulata*	) approx.) approx. 32 mg/kg in) dry food	< 0.01 < 0.01 < 0.01	Opperhuizen *et al*, 1987
PDMS (50 cs) : 35 % **emulsion**	**level 1 :** phytoplankton *Tetraselmis sp.* **Level 2 :** mollusc *Mytilus edulis*	70 mg/l in water direct exposure from water exposure from water and food	 2.08 (BCF) 0.12	Aubert *et al*, 1985; Guillemaut *et al*, 1987
	level 1 : plankton *Tetraselmis sp.* *Artemia salina* **level 2 :** fish *Carassius auratus*	direct exposure from water exposure from food and water	1.9 (BCF) 0.05	
	level 1 : annelid *Nereis diversicolor* **level 2 :** fish *Scorpaena porcus*	direct exposure from water exposure from food and water	0.036 (BCF) 1.4	
	level 1 : annelid *Nereis diversicolor* **level 2 :** crab *Carcinus maenas*	direct exposure from water exposure from food and water	0.036 (BCF) 1.09	
PDMS (100 cs)	chicken White Leghorn	5,000 mg/kg food eggs during exposure and recovery period Chicken at the end of recovery period	**Residues :** < 3 mg/kg < 2 mg/kg kidney, muscle liver < 4 mg/kg fat	Hobbs *et al*, 1975

Thus:

Tetraselmis sp. (phytoplankton) was exposed for 9 days and then fed to *Mytilus edulis* (molluscs) for 12 days.

Tetraselmis sp. and *Artemia salina* (plankton) were exposed for 8 days and then fed to *Carassius auratus* (fish) for 15 days.

Nereis diversicolor (annelids) were exposed for 8 days and then fed to *Scorpaena porcus* (fish) or *Carcinus maenas* (crabs) for 15 days.

The PDMS content of the organisms was measured by atomic absorption spectroscopy after extraction. As in the case of fresh water organisms, PDMS was not bioconcentrated in the phytoplankton and zooplankton, the BCF was < 1 for annelids. The bioaccumulation factor between predators and prey in the food chain was low varying between 0.05 and 1.4, indicating no bioaccumulation of PDMS in the marine food chains studied.

In another study (Hobbs *et al*, 1975), 24 week old White Leghorn chickens were given food containing 200 to 5,000 mg PDMS (100 cs) per kg food for 30 days. The eggs produced during the treatment period and during a 30 day recovery period (PDMS-free diet) were kept for residue analysis. No PDMS was found (detection limit 3 mg/kg). At the end of both treatment and recovery periods, no PDMS was detected in the kidney or the liver of the chickens (detection limit 2 mg/kg), nor in their fat (detection limit 4 mg/kg).

These studies revealed non-detectable levels or negligible concentration of PDMS in body of marine organisms or in certain organs of avians, indicating that PDMS with viscosity greater than 10 cs is not bio-accumulated. PARCOM (1992) concluded that despite the apparently high log P_{ow}, PDMS does not display any potential for bioaccumulation.

SECTION 5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 ENVIRONMENTAL LEVELS

A number of environmental studies have been published in which the authors refer to "siloxanes", "silicones" or "organosilicon compounds"; they assumed that the organic solvent extractable silicon compounds were PDMS.

As mentioned in Section 2.3, the recovery efficiency in studies before 1993 was not satisfactory when extracting PDMS from soil, sediment and sludge, so the findings can be accepted only as approximate indications of the level of PDMS in the environment.

5.1.1 Air

Weschler (1981) identified PDMS (MW > 1900) in the extract from particles from air collected at Pt. Barrow/Alaska. PDMS was analysed by a pyrolysis-GC-MS procedure. The concentration of approx. 8 ng/m^3 was considered "as a guide to the relative amounts of the compounds present". In "field blanks" no PDMS was detected but no detailed description was given of them. Contamination from chemicals and laboratory equipment was excluded. The author suggested that the PDMS-containing particles/aerosols may be generated in distant countries and transported to the sampling point by air currents.

In outdoor air samples from four US cities organosilicon compounds associated with airborne particles were found by Weschler (1988) to be in the order of 1 ng/m^3. The sensitivity of the method was 1 ng.

The top 5 cm peat from a bog in a remote area of North Eastern Ontario/Canada was analysed for organosilicon compounds by Annelin (1991). No peat cutting had been done for the past 30 years. The objective of the study was to investigate atmospheric deposition of organosilicon compounds during the past 30 years. No organosilicon could be detected in the organic solvent extracts (detection limit 0.5 ppm).

5.1.2 Water

Traces of organosilicon compounds have been detected in effluents from WWTP, water samples near WWTP effluents and surface water microlayers near sources of pollution. They were most

probably associated with suspended particles (in most cases water samples were not filtered before extraction and analysis). The extraction (recovery) efficiency of PDMS from water is almost 100%, the low recovery of 69% reported by Watanabe *et al* (1984b) is not explained.

Siloxanes could not be detected in water samples from remote regions (Batley and Hayes, 1991).

Concentrations reported in water have all been in the lower µg/l range (except for point sources effluents) (see Table 5).

5.1.3 Sediment

Extractable organosilicon compounds have been detected at ppm level in sediments from rivers and estuaries in areas known to be polluted with industrial chemicals. In exceptional cases high concentrations have been found; for example Siebert (1988) detected 83 ppm in sediment from the River Rhine and Pellenbarg (1979a) found a maximum of 126 mg/kg in sediments of the New York Bight where sewage sludge has been dumped for many years.

The findings are summarised in Table 6.

5.1.4 Sewage sludge

Because a large number of products containing PDMS are disposed off via drainage systems, significant concentrations of PDMS are associated with sewage sludge in WWTP. Siloxanes up to several hundred mg/kg dry sludge have been reported (Table 7).

5.1.5 Soil

Soil samples taken in the Heidelberg and Soest area of Germany were analysed by AAS after extraction with ether (Siebert, 1988). Recovery efficiencies were not reported , the detection limit was 0.4 mg/kg dried soil (not statistically defined).

Forest soil (depth 0-5 cm)	2/6 samples	0.70 mg/kg	(0.24 - 1.38mg/kg)
Agricultural soil	3/10 samples	0.73 mg/kg	(0.50 - 0.92 mg/kg)
Garden soil	1/3 samples	0.38 mg/kg	
Agricultural soil (S. sludge amended)	3/7 samples	0.43 mg/kg	(0.33 - 0.34 - 0.63 mg/kg)

Table 5 Environmental level of extractable organosilicon compounds in water (concentrations expressed as µg/l water)

Source	Organosilicones µg/l		Detection limit µg/l	Samples with siloxane/total samples	Analytical Method	Recovery efficiency %	Reference
	range	mean					
USA							
WWTP effluent		<6.8[1]	6.8	0/3	AAS	100	ATS, 1985
WWTP effluent	10.8 - 12.7	11.9		4/4	AAS	100	Pellenbarg, 1979b
Surface water microlayer	60.1 - 116.6	84.2		3/3	AAS	100	Pellenbarg, 1979b
AUSTRALIA							
Seawater, polluted		0.8[1]	0.8		ICP	97	Batley and Hayes, 1991
Surface water microlayer near WWTP		4.5[1]	0.8		ICP	97	Batley and Hayes, 1991
Seawater near WWTP		1.8[1]	0.8		ICP	97	Batley and Hayes, 1991
Seawater,unpolluted		<0.8[1]	0.8		ICP	97	Batley and Hayes, 1991
JAPAN							
Rivers, Lakes, Sea							
Nagara River		<2.5[1]	2.5	0/40	AAS		EAJ, 1981
" "	2.0 - 54.2	13.8	0.3	5/9	ICP	69	Watanabe *et al*, 1984b
Dyeing factory effluent	2.6 - 1,150		0.3	3/4	ICP	69	Watanabe *et al*, 1984b
WWTP effluent	2.4 - 4.9	3.6	0.3	2/2	ICP	69	Watanabe *et al*, 1984b

1 only one figure is reported
AAS Atomic Absorption Spectrometry
ICP Inductive Coupled Plasma Emission Spectrometry

Table 6 **Environmental level of extractable organosilicon compounds in sediment (concentrations expressed as mg/kg dried sediment)**

Source	Organosilicones mg/kg		Detection limit mg/kg	Samples with siloxane/total samples	Analytical Method	Recovery efficiency %	Reference
	range	mean					
USA							
Estuaries	0.5-14.8	4.1	0.3	9/15	AAS	33-160	ATS, 1985
Great Lakes District	<0.3-23.7	7.9	0.3	3/6	AAS		ATS, 1985
New York Bight	4.7-126	19.5		14/25	AAS	35	Pellenbarg, 1979a
Potomac River	1.2-8.1	3.6		10/10	AAS	35	Pellenbarg, 1979b
Delaware Bay	0.3-3.0	1.6		9/9	AAS	35	Pellenbarg, 1979b
Chesapeake Bay	1.0-95.2	10.8		27/48	AAS	35	Pellenbarg, 1982
Pudget Sound	0.1-1.0		0.03		ICP	35	Pellenbarg & Carhart, 1990
AUSTRALIA							
Rivers and bays of Sidney area	0.05-1.4	0.3	0.03	9/9	ICP	73	Batley & Hayes, 1991
JAPAN							
All over Japan	1-70	5.8	1	30/40	AAS		EAJ, 1981
Tokyo area	0.3-1.6	0.7		5/6	ICP		SIA, 1982
Nagara River	0.3-5.8	3	0.3	2/9	ICP	58	Watanabe *et al*, 1984b
Urban river	0.75				ICP		Watanabe *et al*, 1985b
GERMANY							
Rivers	0.5-83.1	2.6	0.4	94/114	AAS		Siebert, 1988
Lake Constance	0.6-0.8		0.4	3/26	AAS		Siebert, 1988
North Sea estuary	0.6-0.8		0.4	2/2	AAS		Siebert, 1988

AAS Atomic Absorption Spectrometry
ICP nductive Coupled Plasma Emission Spectrometry

Table 7 Extractable organosilicon compounds in sewage sludge (mg/kg dried sludge)

Country	Organosilicon		Detection Limit	Samples tested	Recovery efficiency (%)	Analytical Method	Reference
	Range	Mean					
USA							
Ann Arbor WWTP		87	0.3	1		AAS	ATS, 1985
Blue Plains WWTP		21	0.3	1		AAS	ATS, 1985
Detroit WWTP		127	0.3	1		AAS	ATS, 1985
Blue Plains WWTP							
Filter cake	60-128	96		9	35	AAS	Pellenbarg, 1979b
Sludge	235-274	254		6	35	AAS	Pellenbarg, 1979b
AUSTRALIA							
Malabar WWTP in Sidney area		364	0.1		74	ICP	Batley and Hayes, 1991
JAPAN							
Night soil treatment (human excretions)		89				ICP	Watanabe *et al*, 1985b
Various WWTPs	34-6,290		0.3	6	58	ICP	Watanabe *el al*, 1984b
GERMANY							
Various WWTPs	65-701	342	0.4	11		AAS	Siebert, 1988

AAS Atomic Absorption Spectrometry
ICP nductive Coupled Plasma Emission Spectrometry

The only sample with extractable organosilicon compounds statistically significantly above the limit of detection was from a forest. The other samples were near or below the limit of detection and were thus of low statistical significance.

Although the PDMS content of soils treated with sludge would be expected to be high since the levels in sewage sludge from German WWTP's is reported to be several 100 ppm, no increased content of extractable organosilicon was found in such soils. The results suggest that PDMS present in sewage sludge amended soils degrade (Siebert, 1988).

5.1.6 Biota

The only data reported have been on fish related to not specified organo silicon compounds. Edible parts of 26/28 fish from various locations throughout Japan were extracted and the Si content analysed by AAS or ICP (Detection limit 1mg/kg). The calculated organosilicon content was 1-16 mg/kg (EAJ, 1981). This result could not be confirmed in a later study in which fish from the same sites were analysed. No organosilicon compounds were detected. (SIA, 1982)

Watanabe *et al* (1984b) detected organosilicon compounds in muscle of carp, barbel and dace from the Nagara River in the range of 0.36 -0.89 mg/kg (recovery efficiency 49%). The inconsistencies of the results may be related to organosilicon compounds other than PDMS or to analytical artifacts as it was reported later by Frye (1988) and by Pellenbarg and Tevault (1988).

5.1.7 Summary-environmental levels

PDMS has been found in waste water. The highest levels (up to several hundred ppm) were detected in sewage sludge. PDMS was reported in the ppb range in effluents from waste water treatment plants or in surface water near such effluents. No organosilicon compounds were detected in water from remote areas. Sediments from polluted water bodies contain a few ppm PDMS.

PDMS was found in the particulate matter of air in the range of a few ng/m^3 and in soil up to 1 ppm.

5.2 HUMAN EXPOSURE

PDMS is used in various applications which lead to direct human exposure e.g. antifoams for food and food processing, personal care products, polishes, cleaners, textile treatment and packaging (see also Section 3.3).

The main routes of direct human exposure to PDMS are therefore oral intake and skin contact.

5.2.1 Oral exposure

Ingestion results from the addition of antifoaming agents containing PDMS to foods like frying oil, jams and marmalades, dry tea and coffee extracts and fruit juice concentrates. The permitted levels of PDMS vary from 3 mg/kg in edible fats and oils to 10 mg/kg in other types of food, depending on the national regulations. The EEC Directive on Food Additives permits PDMS with a viscosity of 350 to 1,050 cs (listed as E900) in all types of food up to a 10 mg/kg level. PDMS of a viscosity of 300 - 1,050 cs at 25°C is cleared under FDA Regulation 173,340 as a defoaming agent for use up to a level of 10 ppm in food with the exception of milk.

PDMS has been evaluated by a joint FAO/WHO Expert Commission on Food Additives (1974). Toxicological data on rat, rabbit, monkey and man were reviewed and it was concluded from studies on PDMS with and without silica (max 5%), that it presented no significant toxicity. Metabolic studies indicated that the orally administered dimethylsiloxanes are mainly excreted unchanged in the faeces. The level of intake causing no toxicological effect was 150 mg/kg bw and an Acceptable Daily Intake (ADI) for man of 1.5 mg/kg bw was set.

PDMS is also used as processing aid during food manufacture but is only present as traces in the final product. PDMS is added either as a pure substance or as an aqueous 10-20% water emulsion to control foam formation, for example, during the washing of fruits and vegetables and in beverage and sweet manufacture.

In the manufacture of food packaging such as paper, paperboard or plastics, PDMS is used as an antifoam or release agent. Extensive residue analyses and migration studies have been carried out to assess the human exposure resulting from these applications. In most cases, no residue was detected in the final product and the migration level into the food or the food simulants was far below that admitted by national or EEC regulations.

5.2.2 Skin Exposure

PDMS is referred to as Dimethicone in the Cosmetics, Toiletries and Fragrances Association list. Its initial use as an additive in cosmetic formulations has been expanded so that it has become major ingredient in some personal care products; it is present in most types of personal care products.

PDMS is also used in consumer products such as polishes and cleaners.

SECTION 6. EFFECT ON ENVIRONMENTAL ORGANISMS

6.1 TOXICITY TO MICRO-ORGANISMS

Few studies have been carried out on bacteria, fungi, algae or protozoa and they have not been well described.

Gettings and Lane (1982) studied the effect of a ^{14}C-labelled hydroxy terminated PDMS (55 cs) spread on the surface of the water or mixed with the sediment in an experimental aquatic ecosystem. Like PDMS, its water solubility is below 1 mg/l. It formed tiny droplets which associated with suspended particulate matter and slowly settled out. The maximum concentration in water was 260 µg/l and the equilibrium concentration 40-50 µg/l. The substance showed no apparent toxic effect on the development of aerobic and anaerobic bacteria or on algae or protozoa after a 24 week exposure.

PDMS dispersed in water (5,000 mg/l) had no effect upon *Escherichia coli* (Firmin, 1984) and a 27% PDMS emulsion did not inhibit activated sludge respiration (Gilliard, 1980) although details were not reported. Wollast (1979) studied the effect of PDMS emulsions on the respiration of activated sludge bacteria since PDMS emulsions are used as antifoaming agents in waste water treatment plants. PDMS (30 and 60 mg/l) had no effect; its concentration was 1,000 times higher than in actual use at WWTPs. Watts *et al* (1993) also demonstrated that PDMS (200 cs) had no effects on the activity of aerobic and anaerobic sludge microorganisms of waste water treatment plants.

Samples of beech wood impregnated with PDMS (concentration not reported) were inoculated with meadow soil and stored for 39 days under conditions of humidity and temperature favourable to the development of fungi. Treated samples and controls were similarly invaded by numerous species of fungi (Sharp *et al*, 1970).

Dive (1981) demonstrated the absence of toxicity of PDMS (50 cs; concentration not reported) to the protozoan *Colpidium campilum*.

In conclusion, no toxic effect of PDMS has yet been demonstrated with bacteria, algae, protozoa and fungi.

6.2 TOXICITY IN AQUATIC MEDIA

As presented in Section 4.4, large molecules such as PDMS are not taken up by fish or other aquatic organisms, so, a systemic effect is not expected. Toxicological effects depend on the concentrations of substance in the test media (water, sediment). As PDMS is extremely hydrophobic it tends to sorb strongly to solid particles (soil, sediments) or to glassware (Hobbs *et al*, 1975) making it difficult to measure and to maintain constant exposure concentrations in solution. Therefore in many studies nominal concentrations or saturated solutions have been used. To study the effects of PDMS concentrations higher than the water solubility PDMS has also been tested in emulsion form.

6.2.1 Fish

The results are summarised in table 8.

In water saturated with PDMS (50, 100, 350, 12,500 cs) no acute toxic effects were reported (Maggi and Alzieu, 1977 ; Hill *et al*, 1980b). The toxic effects of PDMS emulsions at high concentrations were shown to have been caused by the emulsifier used in the formulation (Hobbs *et al*, 1975; Aubert *et al*, 1985).

In prolonged tests emulsions have been used. Firmin (1984) reported that 88 mg/l emulsified PDMS (50 cs), produced a slight agitation in *Pleuronectes platessa* (plaice) after 96 hours. Cabridenc (1978) exposed *Phoxinus phoxinus* (minnows) to 3,000 mg/l PDMS (viscosity not specified) for 8 days without feeding or aeration. Under these unusual test conditions 40% of the fish died.

Hill *et al* (1984) studied the toxicity of a PDMS (50 cs) emulsion in a dynamic test on embryos and larvae of *Cyprinodon variegatus* (Sheepshead minnow); controls were exposed to the emulsifier. After 33 d, the PDMS emulsion was found to have less effect than the emulsifier on larval survival, size and body weight.

Salmo gairdneri (Rainbow trout) were fed with food containing PDMS (350 cs) for 28 days. It was estimated that 10 mg of PDMS per fish was ingested per day, corresponding to 10,000 mg/kg bw. After 28 days exposure the fish received untreated food for a further 14 days. The water was renewed twice a week. No mortality or change in behaviour or growth relative to the control fish was observed. Histopathological examination of skin, muscle, liver, bile, adrenal, stomach and gut revealed no abnormalities. (Mann *et al*, 1977)

Table 8 Fish Toxicity

SPECIES	PRODUCT	RESULTS[1]	REFERENCE
		FRESH WATER	
Lepomis macrochirus *Salmo gairdneri*	PDMS (350 cs) 30 % **emulsion**	LC_{50} - 96 h > 3,000 mg/l and hypoactivity from 300 mg/l	Hobbs *et al*, 1975
Phoxinus phoxinus	PDMS (visc. not specified)	LC_{40} - 8 d = 3,000 mg/l	Cabridenc, 1978
Salmo gairdneri	PDMS (350 cs) 25% in food during 28 d; followed by 14 d observation period	no effect on behaviour and growth with 10 mg PDMS/fish/d	Mann *et al*, 1977
		SEA WATER	
Pomatoschistus minutus *Gasterosteus aculeatus*	PDMS (100, 350 and 12 500 cs)	no mortality - 96 h at saturation	Maggi and Alzieu, 1977
Fundulus heteroclitus	PDMS (350 cs) 30% **emulsion**	LC_{50} - 96 h> 300 mg/l LC_{0} = 30 mg/l	Hobbs *et al*, 1975
Scorpaena porcus	PDMS (50 cs) 35% **emulsion**	LC_{50} - 50 h = 700 mg/l	Aubert *et al*, 1985
Carassius auratus	PDMS (50 cs) 35% **emulsion**	LC_{50} - 24 h = 3,500 mg/l	Aubert *et al*, 1985
Pleuronectes platessa	PDMS (50 cs)	toxicity - 96 h > 10,000 mg/l at the surface of water (5mg/l in water)	Hill *et al*, 1980b
Pleuronectes platessa	PDMS (50 cs) 20% **emulsion**	toxicity - 96 h > 88 mg/l	Firmin, 1984
Cyprinodon variegatus	PDMS (50 cs) 35% **emulsion**	235 mg/l during 33 d : Slight decrease of hatchability of embryos Effect on survival, length and weight of larvae smaller than effect of corresponding amount of emulsifier	Hill *et al*, 1984

1 Values represent the concentration of pure PDMS

Thus, PDMS produced no acute and chronic toxic effects when dispersed in water. In an emulsion, the observed toxicity can be attributed to the emulsifying agent.

6.2.2 Invertebrates

Crustacea

Results are shown in table 9.

Table 9 Crustacean Toxicity

SPECIES	PRODUCT	RESULTS	REFERENCE
FRESH WATER			
Daphnia magna	PDMS (100 cs)	48 h - LC_{50} 44.5 mg/l[1] as layer on surface	Hobbs *et al*, 1975
Daphnia magna	PDMS (350 cs), emulsion	48 h - LC_{50} 1000 mg/l emulsion	Spacie, 1972
Daphnia magna	PDMS (350 cs), 30% emulsion	48 h - LC_{50} 73.4 mg/l[1]	Hobbs *et al*, 1975
SEA WATER			
Artemia salina *Palaemonetes varians* *Clinabarius misanthropus*	PDMS (100, 350 and 12,500 cs)	no mortality 96 h at saturation	Maggi *et al*, 1977
Artemia salina *Carcinus maenas (crab)*	PDMS (50 cs), 35% emulsion	LC_{50} - 9 d > 7,000 mg/l[1] mortality - 10 d > 3,500 mg/l[1]	Aubert *et al*, 1985
Pachygrapsus crassipes	PDMS (350 cs), 30% emulsion	LC_{50} - 96 h > 300 mg/l[1]	Hobbs *et al*, 1975
Peneaeus oxtecus *Carcinus maenas (crab)*	PDMS (50 and 100 cs), emulsion	no effect at 100 mg/l emulsion on respiration after 50 to 80 min and osmoregulation at 8h	Houvenaghel, 1980

1 Values represent the concentration of pure PDMS

In common with other low density immiscible liquids, PDMS forms a surface film on water if added at concentrations which exceed the water solubility. This film can cause physical entrapment of *Daphnia*; but this is not a toxic mechanism.

Some studies have been conducted with PDMS at concentrations considerably greater than the water solubility, resulting in a surface film. Hobbs *et al* (1975) observed entrapment of *Daphnia* exposed to PDMS (100 cs) and reported an EC_{50} value of 44.5 mg/l.

Where *Daphnia* has been tested with PDMS (50, 350 and 1,00 cs) concentrations lower than the water solubility (50-100 ppb), no surface entrapment or mortalities have been observed (Annelin *et al*, 1994).

Where there is a requirement to test above the water solubility, OECD Test Method 202 states that the product may be tested as a stable emulsion. Spacie (1972), tested a PDMS (350 cs) emulsion and reported an EC_{50} (48 h) value of 1,000 mg/l. In a later study Hobbs *et al* (1975) found that the same viscosity PDMS Fluid (350 cs) displayed an EC_{50} (48 h) of 73.4 mg/l. However, the potential toxicity of the emulsifying agent was not taken into consideration.

Stable emulsions with PDMS concentrations greater than the EEC labelling criteria value of 100 mg/l have been generated using the emulsifying agent Tween 80. A range of viscosities have been tested from 10 cs to 60,000 cs and all show a No Observed Effect Level of > 200 mg/l (Klein *et al*, 1994).

PDMS was not found to exhibit toxic effects (Hobbs *et al*, 1975; Maggi *et al*, 1977; Aubert *et al*, 1985) or influence physiological regulation (Houvenaghel, 1980) in marine species such as crabs and shrimps.

In conclusion, there is no evidence that PDMS dissolved in water or in emulsion form causes toxicity to crustacea. In the event that testing is conducted at concentrations greater than the water solubility and a surface film is formed, small crustacea (e.g. *Daphnia*) may be entrapped.

Molluscs

The findings in sea water molluscs are presented in Table 10.

Sea water saturated with PDMS fluids (100, 350 and 12,500 cs) did not kill *Ostrea edulis* (European Oyster) *Mytilus edulis* (mussel sp.) and *Littorina littorea* (periwinkle) during a 96 hour exposure (Maggi and Alzieu, 1977). With *Mytilus edulis* no mortality was observed at PDMS (50 cs) concentrations far above the water solubility (Hill, 1980a).

A 35% emulsion of PDMS (50 cs) was not lethal to *Mytilus edulis* (mussel) after 10 days at 700 mg/l PDMS (Aubert *et al*, 1985) and the LC_{50} (96 h) was 1,980 mg/l with a 20 % emulsion (Hill, 1980a).

The action of PDMS on physiological functions of *Mytilus edulis* was studied by Houvenaghel (1980). Its filtering capacity, evaluated by measurement of the rate of filtration during 120 minutes of a 0.001 % neutral red suspension, was not modified by the addition of 100 mg/l PDMS (unspecified viscosity) adsorbed on a 30 μm starch suspension. This absence of effect was

confirmed by an absence of effect on osmoregulation measured by the chloride content of haemolymph.

Table 10 Mollusc Toxicity

SPECIES	PRODUCTS	RESULTS[1]	REFERENCE
SEA WATER *Ostrea edulis* *Mytilus edulis* *Littorina littorea*	PDMS (100; 350; 12,500 cs)	no mortality - 96 h at saturation	Maggi *et al* , 1977
Mytilus edulis	PDMS (50 cs) 35% **emulsion**	LC_{50} - 96 h (3,500 mg/l) LC_{50} - 80 h (10,000 mg/l emulsifying formulation without PDMS) no mortality - 10 d (700 mg/l)	Aubert *et al*, 1985
Mytilus edulis	PDMS (50; 100; 550; and 1000 cs) absorbed on 30 μm starch particles	no effect at 100 mg/l on filtering activity at 2h	Houvenaghel *et al*, 1980
Mytilus edulis	PDMS (50; 100; 550 and 1,000 cs) **emulsions**	slight effect at 100 mg/l **emulsion** on filtering activity and no effect on osmoregulation	Houvenaghel *et al*, 1980
Mytilus edulis	PDMS (50 cs) PDMS (50 cs), 20% **emulsion**	LC_{50} - 96 h (>1,020 mg/l) LC_{50} - 96 h (1,980 mg/l)	Hill, 1980a Hill, 1980a

1 Values represent the concentration of pure PDMS

The results suggest that PDMS fluid have no effect on molluscs.

Annelids

Tests were carried out with the annelid *Nereis diversicolor*. These tests are of special interest as these organisms live buried in the sediment, so that the toxic risk of products adsorbed on particles can be readily evaluated.

Sediment mixed with 10,000 and 1,000 mg PDMS (50 cs)/kg had no effect on burrowing activity of annelids after 96 hour and after 28 days respectively (Craig and Caunter, 1990). Similar results were found by Aubert *et al* (1985) with sea water to which a PDMS (50 cs) emulsion containing

35% PDMS was added. With 350 mg/l no lethal effect was observed upon *Nereis diversicolor* during 9 days and the toxicity observed with a 3,500 mg/l concentration is explained by the emulsifier alone. After 9 days exposure to 700 mg/l, PDMS had no effect on the growth as compared controls.

6.2.3 Algae

In Windhock/Namibia, Van der Post (1978; 1979) observed a reduced growth of algae in a sewage maturation pond. Based on experiments with a commercial product containing some undefined PDMS, the author assumed that the effect was related to hydrolysis of PDMS to trimethyl- and dimethyl-silanols. No proof for the hydrolysis was given. This study has been reviewed by Smith (1980) who reported that the structures of PDMS given by Van der Post wee misinterpreted and the postulated reactions contradictory to all PDMS chemistry. Other studies described below could not confirm any effect of PDMS to algae.

Aubert *et al* (1985) studied the effect of a 35% emulsion of PDMS (50 cs) (containing 6% emulsifier) during a 9 day exposure period. Control tests used 6% emulsifier in water. At the lowest concentration of 1,000 mg/l emulsion (350 mg/l PDMS) the algae population was steady; no growth was observed. The same occurred with controls. At higher concentrations the cell count was reduced. The authors reported the results in terms of the LC_{50} as the time for 50% survival at fixed concentrations:

Exposure period for 50% survival in:	**Concentration mg/l**		
	2,000	4,000	10,000
PDMS **emulsion**	120 h	80 h	75 h
emulsion without PDMS	170 h	120 h	96 h

Saturated solutions of PDMS (100, 350 and 12,500 cs) had no inhibitory effect on the growth of two flagellae *Dunaliella tertiolecta* and *Tetraselmis suesica* and two diatomeae *Phaeodactylum tricornutum* and *Gyrosigma spencerii* during a 9 day exposure period. The saturated solutions were prepared by violently stirring 10 ml of each PDMS in 1l water for 12 hours and decanting the overlying phase. The PDMS concentration in water was not measured. To 9.5 ml of the saturated solution 0.5 ml of the respective phytoplankton cultures were added and the growth observed. Controls were included. A film of PDMS spread at the surface of the water did not disturb the growth of *Gyrosigma spencerii* (Maggi and Alzieu, 1977).

6.2.4 Conclusion

From the available data on various aquatic species it can be concluded that no toxic effects are related to the presence of PDMS.

6.3 TOXICITY TO TERRESTRIAL ORGANISMS

6.3.1 Higher Plants

Effects of sewage sludge containing ^{14}C-PDMS on arable soil was examined. Two cereals were sown sequentially, springwheat followed by soybeans, and the following observations were made during a 7 month period: germination of the seeds growth, uptake of soil nutrients by plants in roots, shoots and grains. No significant difference from controls were observed (Battelle, 1992a).

The effect of PDMS (10 cs) (10% emulsion) as an aerial antitranspirant treatment of a conifer plantation was studied by Belt *et al* (1977). When applied at about 30 ml/m^2 this treatment had no immediate serious repercussion on vegetation and no significant difference was observed after regeneration the following year.

6.3.2 Insects

The insecticide activity of PDMS (5 to 1,000 cs) was evaluated by direct application of 5 µl pure substance to the ventral thorax of adult *Acheta domesticus* (cricket) (Levier, 1988). The time of loss of righting reflex increased with the viscosity of the PDMS and the mortality at 48 hours decreased 2 fold when the viscosity of PDMS increased 200 fold. A similar effect of PDMS (10 cs) was observed by Nielson *et al* (1975).

6.3.3 Birds

Hobbs *et al* (1975) studied the subacute toxicity of a PDMS (100 cs) incorporated at various levels in the food of young *Anas platyrhynchos* (Mallard duck) and *Colinus virginatus* (Bobwhite quail). The birds were fed for 5 days with the contaminated diet and kept 3 additional days on a standard food for observation. At the highest concentration in the diet (5,000 mg/kg food) no mortality and no other signs of toxicity occurred. The effect of this PDMS was also studied on the reproduction of 24 week old White Leghorn chickens, fed with a diet containing 0, 200, 1,000 or 5,000 mg of PDMS/kg feed. When the hens were at least 28 week old, the eggs were collected, weighed and their quality checked. In each group one hundred eggs were randomly selected to study hatchability and the viability of the chicks, kept for a 30 day period and fed with the basal diet. At

the highest level of PDMS in the diet, no significant effect was observed on eggs production and quality. The weight and the viability of the chicks were not affected by the treatment.

These experiments support the conclusion that PDMS are not toxic to birds by ingestion.

6.4 CONCLUSIONS

Studies on the effect of PDMS on organisms in the environment demonstrate they have no adverse effects or if any only very limited toxic effects.

SECTION 7. KINETICS AND METABOLISM

Several studies have been carried out to examine the oral absorption of PDMS (35 cs to 1,200 cs). These show that PDMS is not significantly absorbed from the gastrointestinal tract and is rapidly eliminated unchanged by faecal excretion.

Polymeric siloxanes containing reactive groups (e.g. vinyl groups) may induce reactions with other biological molecules after subcutaneous injection (Garrido *et al*, 1993). However these compounds are not subject of this report as defined in Section 2.

Dietary doses reported in the literature as mg/kg or percentage in the food, have been converted in this report into mg/kg bw using standard conversion factors.

Animal Studies

An aqueous emulsion containing about 11% of ^{14}C labelled PDMS (1,200 cs) was administered orally to two dogs (25,000 mg) and one rat (580 mg). The animals were killed 24 hours later and tissues analysed for ^{14}C PDMS. The amount of PDMS absorbed from the gastro-intestinal tract was of the order of 0.001%. A second rat received an intramuscular injection (500 mg) of the ^{14}C PDMS (1,200 cs) fluid. No radioactivity was detected in the samples of exhaled CO_2 collected periodically over one week. Most of the ^{14}C was present in the intestinal contents (Chenoweth *et al*, 1956).

Another study evaluated the absorption, tissue distribution and excretion of ^{14}C PDMS, (100 cs) in rats (Siddiqui *et al*, 1984). Three male Sprague-Dawley rats (210-230g) were given orally a single dose of approximately 830 mg/kg bw of ^{14}C PDMS (100 cs), corresponding to 48 mg radiolabelled material per rat. Each animal was immediately placed in a metabolism cage for collection of expired air and excreta for 6 days. Plasma, expired air, urine, faeces and tissues were analysed for ^{14}C activity by liquid scintillation counting. The total 6 day faecal excretion of ^{14}C material was approximately 96% of the administered dose. The peak ^{14}C activity-excretion occurred during the first 48 hours. Trace amounts of radioactivity (0.05% of the administered dose) were detected in liver, kidney and lung following the 6 day study period, and no radioactivity was detected in the other tissues or organs (spleen, heart, adrenal, testes, skeletal muscle or fat). No ^{14}C derived activity was detected in the samples of plasma, expired air or urine that were collected at various intervals.

In an extensive study by Annelin *et al* (1989), single and repeated oral dose experiments were carried out to determine the pharmacokinetics of PDMS (35 cs and 1,000 cs). Male Sprague-Dawley rats (250-350g) were administered 250 or 2,500 mg/kg bw (0.5% or 5% in the food) ^{14}C labelled PDMS fluid as one or more doses. In the repeated dose study, animals were fed at dietary levels providing daily doses of 250 and 2,500 mg/kg bw of unlabelled PDMS for 13 days, followed by a single oral dose of radiolabelled PDMS on day 14. As no radioactivity had been detected in expired air in a range-finding study, urine and faeces only were collected at 4, 8, 12, 24 and 48 hours after dosing. From the single dose groups, four animals were killed at each of four time points (4, 8, 24, 48 h) after oral administration.

All animals receiving repeated doses were killed 48 hours after receiving the radioactive PDMS. Urine, faeces and the following tissues and organs were analysed by liquid scintillation counting for ^{14}C activity: stomach, stomach contents, caecum, caecal contents, large intestine, large intestinal contents, liver, spleen, lungs, heart, kidneys, testes, brain, sub-mandibular lymph nodes, tracheobronchial lymph nodes, mesenteric lymph nodes, sternum, peritoneal fat and skeletal muscles from the thigh area. In all groups, the bulk of the test material was found in the gastrointestinal tract or in the faeces. By 24 hours, essentially all the material was found in the faeces. Slight radioactivity was measured in the urine - less than 0.2% for the animals receiving a single 2,500 mg/kg bw dose of PDMS (35 cs). In tissue samples, less than 0.2% of the administered dose was measured at 4 hours and 8 hours after sacrifice. No radioactivity was detected after 48 hours in any tissue or organ. Minor leakage (2.3% of the administered dose of PDMS (35 cs) at the higher dose rate) from the anus without incorporation into faecal material, was observed during the study. The results of the repeated dose experiment were essentially the same as those of the single dose experiments. The absence of detectable levels of PDMS fluid in tissues at 24 hours and 48 hours indicated that, if absorbed at all, PDMS fluid was rapidly eliminated. In order to determine whether there was any change in the test material during passage through the gastro-intestinal tract, samples of faeces from animals that received 35 cs fluid at 2,500 mg/kg bw were analysed by chromatography and compared to the initial solutions. The results indicated that there was no shift in molecular weight and that no metabolites or rearrangement products were present.

Due to the absence of absorption through the gastro-intestinal tract, other routes of exposure (e.g. intra-peritoneal or subcutaneous) have been used to determine the 'Minimum Toxic Dose' (See Section 8, particularly teratogenicity studies).

SECTION 8. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO SYSTEMS

Introduction

PDMS of all viscosities display a low acute toxicity via oral, dermal or inhalation routes of administration. Many of the early studies were conducted on substance of unknown purity. With the exception of one study (Kumar *et al*, 1984) in which there was clear evidence that toxic effects were attributable to impurities not characteristic of commercially available PDMS, the general absence of toxic effects supports the view that impurities present have no significance toxicologically.

Although there is a large volume of toxicological data to support medical applications of silicones, these studies have been conducted using specially purified PDMS. They are therefore not considered to be representative of commercially available PDMS which is sold for all other industrial and consumer applications. These studies have therefore not been included in this report.

8.1 ACUTE TOXICITY

8.1.1 Oral

The oral LD_{50} of PDMS has never been reached, guinea pigs and mice, even with excessive dosing.

Tests performed in guinea pigs and rats indicated a low order of toxicity (Table 11). The only adverse effect was of loose stools which was more apparent with low viscosity fluid (Rowe *et al*, 1948).

8.1.2 Dermal

No toxic effects were observed in rabbits following acute dermal exposure. Application of 19,400 mg/kg bw PDMS (350 cs) under an occlusive dressing to the clipped skin of four male New Zealand rabbits for 24 hours caused no adverse effect or evidence of irritation. This was the maximum volume of liquid which could be tested using this method. The dermal LD_{50} value in rabbits is therefore > 19,400 mg/kg bw (Union Carbide, 1953). Similar experiments in Hillstop-Wistar rats using a 4 hour exposure period revealed no toxic effects at 32,000 mg/kg bw (Union Carbide, 1978).

Using PDMS (50; 500 and 1,000 cs), Rondot (1985b,c,d) found that the dermal LD_{50} in rats was greater than 2,000 mg/kg bw. Finally Plotzke and McMahon (1994) demonstrated in an *in vitro* test that ^{14}C-PDMS (350 cs) does not penetrate through the male rat skin;

Table 11 Acute oral toxicity data for PDMS

Viscosity (cs)	Species	LD_{50} (mg/kg)	Reference
10	Rat	> 4,990	Monnot, 1982
20	Rat	> 2,000	Rondot, 1985a
50	Guinea Pig	> 47,750	Rowe *et al*, 1948
100	Rat	> 4,800	Löser, 1981
140	Rabbit/Dog/Cat	> 9,800[2]	Gloxhuber and Hecht, 1955, 1956
140	Rat	> 19,400	Gloxhuber and Hecht, 1955, 1956
350	Rat	> 48,600	Rowe *et al*, 1948
350	Rat	> 48,600	Union Carbide, 1953, 1978
950	Rat	> 9,800	Jackson, 1979
ND[1]	Rat	> 24,000	Clark *et al*, 1979
1,000	Rat	> 4,800	Bomhard, 1983

1 No data on viscosity
2 These results were based on single animals

8.1.3 Inhalation

No signs of inhalation toxicity with PDMS have been observed in animals. Exposure of dogs, guinea pigs and rats to an aerosol (particle size not specified) of PDMS (300 cs) for 6 hours at a nominal concentration of 2.12 mg/l (equivalent to 2.12 g/m^3) showed only minimal signs of discomfort (Calandra *et al*, 1976).

Experiments have also been conducted under conditions which simulated pharmaceutical applications. Exposure of rabbits to an aerosol containing 5% PDMS (12,500 cs) mixed with 95% chlorofluorocarbon (Freon 115 and Freon 12) delivered as a 'burst' from a self pressurised aerosol spray can, for 30 seconds every half an hour for 7,5 hours resulted in no adverse effects on survival, behaviour or gross pathology of the rabbits (Calandra *et al*, 1976). No supporting analyses were conducted.

In a recent study carried in accord with OECD Guideline No 403, the acute inhalational toxicity was determined in Wistar rats (Pauluhn, 1990). Due to the very low volatility of 10,000 cs PDMS, an

aerosol was generated using a 25% solution in dichloromethane (10 ml/m^3). Groups of 5 male and 5 female Wistar rats were exposed to nominal concentrations of 200, 500, 1,000 and 2,500 mg/m^3 for 4 hours (measured concentration were 125, 322, 445 and 695 mg/m^3 respectively). The Mean Mass Aerodynamic Diameter (MMAD) was 1.3 - 1.8 μm, with an average particle size of < 3 μm. The corresponding control groups were exposed to dichloromethane alone. No deaths or untoward symptoms were reported. The highest dose administered, 695 mg/m^3 was found to be the No Observed Effect Level (NOEL). In a similar experiment (Pauluhn, 1985), the acute inhalational toxicity of PDMS (100,000 cs) was evaluated but to generate the aerosol, a 25% solution in white spirit was used. Groups of 5 male and 5 female Wistar rats were exposed to nominal concentrations of 5,000 and 18,750 mg/m^3 (measured concentration of 4,315 and 11,582 mg/m^3 respectively). Solvent control animals were exposed to nominal concentrations of 250,000 and 500,000 mg/m^3 of white spirit respectively. The MMAD was 1.5 μm and 100% of particles were <5 μm. The 4 hour LC_{50} value of the aerosol of PDMS (100,000 cs) was greater than 11,580 mg/m^3. At the top dose mortalities were observed in both the test and solvent control groups.

In conclusion these studies show that inhalation exposure to a PDMS aerosol causes no observed adverse effects which can be attributed to the test compound.

8.1.4 Intraperitoneal

The intraperitoneal LD_{50} of PDMS (350 cs) in New Zealand rabbits was greater than 2,000 mg/kg bw (Stanton, 1983). Animals were killed 48, 72, 96 and 120 hours after administration of the test substance. No deaths or overt signs of toxicity were observed. There were no adverse effects in the lungs or other viscera.

PDMS (350 cs) was administered by intraperitoneal injection to Charles River mice at a dose level of 50 ml/kg bw (48,600 mg/kg bw), control animals were injected with cottonseed oil. Three test and two control groups, each of 5 animals, were used in the study. Each animal was observed immediately after dosing and after 4, 24, 48 and 72 hours. No adverse reactions or symptoms were observed (Henrich and McMahon, 1990). The intraperitoneal LD_{50} in mice is therefore greater than 48,600 mg/kg bw.

The effect of a single intraperitoneal dose of PDMS (50, 350 and 12,500 cs) was also observed over a 90 day period. Rowe *et al* (1948) administered 0.1, 0.3, 1.0, 3.0 and 10 ml/kg bw to rats (group numbers not specified). No inflammation was observed, but nodules, characteristic of a foreign body reaction, developed in the omental tissue and on the surface of the liver, spleen and diaphragm. As a follow up, groups of 5 male rats each received 0.5 and 1.0 ml/rat of 50, 350 or

12,500 cs PDMS fluids or mineral oil or olive oil. No systemic effects were noted either during the study or at the 90 day study termination.

In a similar experiment Gloxhuber and Hecht (1955, 1956) administered PDMS (60 or 140 cs), or a PDMS (75 cs) emulsion to rats or mice (number of animals not specified) at a single dose level of 10 ml/kg bw by intraperitoneal injection. Eight animals died later than 1 year after injection; autopsy revealed no evidence of tumours in any of these animals. In all cases the PDMS did not remain free in the abdominal cavity but dispersed into fine droplets and was deposited in the peritoneal tissues where it produced mild granulomatous reactions.

8.1.5 Subcutaneous

Subcutaneous injection of PDMS of varying viscosity produced no overt toxicity. Rowe *et al* (1948) injected 0.1 ml of 50 or 350 cs PDMS subcutaneously into an area on the back of a rabbit the hair of which had been removed by clipping. Observations were made at 5, 24 and 48 hours. No irritation or other signs of toxicity were apparent. A similar absence of toxicity in mice was noted by Gloxhuber and Hecht (1955, 1956).

In a later study, Olson and Sadek (1962) compared the effects of a subcutaneous injection of 0.3 ml sterile 10, 20, 50 and 100 cs fluids on the backs and bellies of rabbits. The animals were observed 24 hours after injection. There were no effect on gross, or histo-pathological effects but a mild inflammatory response was observed at the injection site.

Similar results were reported by Calandra *et al* (1976).

8.1.6 Intradermal

Intradermal injection of PDMS of varying viscosities produced no evidence of toxicity. Rowe *et al* (1948) and Calandra *et al* (1976) administered 0.1 ml of 50, 350 or 12,500 cs fluid by intradermal injection into the clipped skin on the back of a rabbit. During a 7 day observation period no deaths occurred and there was no evidence of irritation or other toxicity. Blebs formed by the higher viscosity fluids disappeared within one week without residual evidence of tissue damage.

PDMS fluid (350 cs) was administered by intradermal injection to male New Zealand rabbits (Henrich and McMahon, 1990). The dorsal skin was clipped and 2 animals each received five 0.2 ml injections of the test substance or a cottonseed oil control at separate sites on either side of

the spinal cord. Each injection site was examined at 24, 48 and 72 hours after injection for evidence of erythema and oedema; none was observed.

8.1.7 Intravenous Injection

Several studies carried out before 1970, evaluated the acute toxicity of PDMS (100, 350 and 1,000 cs) by intravenous injection (Reed and Kittle, 1959; Fitzgerald and Malette, 1960; Badura *et al*, 1968) to examine the suitability of PDMS as an antifoam in gas debubblers used for the oxygenation of blood during surgery.

With the exception of the study by Fitzgerald and Malette (1960) in which no deaths were observed, the intravenous LD_{50} in dogs was less than 1.0 ml/kg (equivalent to 970 mg/kg). In most cases death occurred rapidly following injection; dyspnoea, hypotension and tachycardia, together with the histopathological findings support the conclusion that death occurred as a consequence of PDMS causing pulmonary embolism. This is attributed to direct physical blockage of the blood vessels rather than secondary to a toxic effect. Thus although these studies indicate that intravenous injection of large quantities of PDMS can, in common with other water-insoluble chemicals administrated via this route, cause death by pulmonary embolism, this is not considered to be relevant in the assessment of toxic hazards from other routes of exposure to PDMS.

8.2 IRRITATION AND SENSITISATION

8.2.1 Skin Irritation

The findings in skin irritation studies conducted on PDMS fluids of varying viscosities are presented in Table 12.

Techniques have varied from a single exposure for 24 hours (Palazzolo, 1964) to 20 repeated exposures over a 28 day period. With the exception of Badinand (1952) and Kumar *et al* (1984) who used guinea pigs, the test animal was the rabbit. No evidence of irritation was observed on exposure of intact or abraded skin to single or repeated doses of PDMS. In a poorly documented study, Guillot *et al* (1979) reported that applications over 56 days led to a slight inflammatory reaction of the skin; this can not be considered of significance to the evaluation of the acute skin irritation potential of PDMS.

8.2.2 Eye Irritation

PDMS of various viscosities have been evaluated for eye irritation potential in many studies (see table 13). Direct instillation of PDMS (typically 0.1 ml) produced transient discomfort but no significant signs of irritation in rabbits (Rowe *et al*, 1948; Clark *et al*, 1979; Guillot *et al*, 1979; Kellner *et al*, 1982). The only adverse effect occurred with low viscosity fluid. Industrial Biotest Laboratory (1967) reported 10 cs fluid to be mildly irritating. In a comparison of 50, 350 and 12,500 cs fluids, Rowe *et al* (1948) found that the transitory conjunctival irritation which developed a few hours after contact, disappeared within 24 hours; with a lower viscosity fluid (50 cs) the eye had returned to normal within 8 hours. A wide range of fluid viscosities were studied by Julou *et al* (1973); no irritation was observed in any of these tests.

Kumar *et al* (1984) referred to the eye irritancy of 5 samples of PDMS (100 cs) produced in India and tested in guinea pigs and rabbits (3 animals per test). Significant mortality was observed in both species when two samples of high acidity were instilled; these clearly contained unusual impurities. No eye irritation was observed with the other samples. In view of the uncharacteristic nature of these samples the results are not considered appropriate for evaluating the irritation potential of commercially available PDMS.

In a repeat dose experiment over 20 days (volume and total number of applications not specified), Badinand (1952) reported that PDMS (2,000 cs) caused slight erosion of the cornea (methods of evaluation not quoted) in guinea pigs (number of animals not specified); the eyes returning to normal after a 15 day recovery period. The effect of prolonged contact (3-6 h) of PDMS (500; 1,000 and 12,500 cs) on the eye has also been studied by Refojo *et al* (1985) in rabbits; there was no evidence of irritation in any of the animals.

In conclusion, PDMS fluid of a wide range of viscosities displays no potential to cause eye irritation following single exposure, although contact with low viscosity liquid may cause transitory conjunctival redness. This may be due to the physical effect of the silicone causing disruption of the tear film and hence producing a 'dry eye' effect. Atypical contact over a prolonged period may cause more marked irritation (see also Section 5.2 on human exposure).

8.2.3 Vaginal Irritation

PDMS is used as a condom lubricant. Vaginal irritation studies are therefore particularly important for evaluating this potential route of human exposure.

Table 12 Summary of Skin Irritation Tests on PDMS

Viscosity (cs) of PDMS used (Pure material)	Species	No. of animals	Volume applied (ml)	Type of application	No. of applications	Test Duration (days)	Effects	Reference
10	Rabbit	3	N.D.	semi occlusive (continuous application to intact skin)	10	14	Non irritating	Calandra *et al*, 1976
50	Rabbit	3	N.D.	semi occlusive (continuous application to intact skin)	10	14	Non irritating	Stanton, 1984
50	Rabbit	N.D.	N.D.	repeated application to the ears and a semi occlusive dressing applied to the shaved belly of the rabbits	20	28	Non irritating	Rowe *et al*, 1948
100	Rabbit	2	0.5	applied to the ears under an occlusive dressing	1	1	Non irritating	Thyssen, 1980.
100	Rabbit	3	0.5	Draize method	10 (daily)	15	Non irritating	Kumar *et al*, 1984
100	Guinea pig	3	0.5	Draize method	10 (daily)	15	Non irritating	Kumar *et al*, 1984
350	Rabbit	4	0.5	continuous occlusive dressing to intact and abraded skin	1	3	Non irritating	Palazzolo, 1964
1,000	Rabbit	3	0.5	Draize method, OEDC Guideline 404	1	7	Non irritating	Suberg, 1984a
2,000	Guinea pig	N.D.	N.D.	N.D.	20 (daily)	20	Non irritating	Badinand, 1952
100,000	Rabbit	N.D.	N.D.	N.D.	N.D.	N.D.	Non irritating	Gonnet and Guillot, 1985
N.D.	Rabbit	3	0.5	Draize test : intact and abraded skin	1	3	Non irritating	Clark *et al*, 1979
ND Pure and 10 % aqueous emulsion	Rabbit	3	N.D.	Applied daily on flanks. Excess was wiped off after 30 seconds	repeated	56	Slight inflammatory reaction	Guillot *et al*, 1979

N.D. No Data

Kumar *et al* (1984) observed that PDMS (100 cs) of comparable purity to commercially available PDMS was non-irritating to the vagina (as measured by the absence of inflammatory leucocytes in vaginal smears) of female rats. Two samples of PDMS with high acidity values, indicative of unusual impurities,caused irritation.

Table 13 Summary of Acute Eye irritation Test on PDMS

PDMS viscosity (cs)	Species	No. of animals	Volume applied (ml) single dose	Effects	Reference
10	Rabbit	N.D.	N.D.	Mildly irritating All symptoms resolved within 48 h	Schoenig *et al*, 1967
20	Rabbit	6	0.1	Non irritating	Gonnet and Guillot, 1985
50	Rabbit	N.D.	N.D.	Non irritating	Rowe *et al*, 1948
100	Rabbit	1	N.D.	Non irritating	Olson, 1957
100	Rabbit	6	0.1	Non irritating	Julou *et al*, 1973
350	Rabbit	N.D.	N.D.	Midly irritating	Industrial Biotest Lab., 1967
350	Rabbit	N.D.	N.D.	Non irritating	Rowe *et al*, 1948
350	Rabbit	6	0.1	Non irritating	Julou *et al*, 1973
500	Rabbit	N.D.	0.7 - 1.0	Non irritating	Refojo *et al*, 1985
1,000	Rabbit	N.D.	0.7 - 1.0	Non irritating	Refojo *et al*, 1985
1,000	Rabbit	6	0.1	Non irritating	Kellner *et al*, 1982
1,000	Rabbit	3	0.1	Non irritating	Suberg, 1984b
1,000	Rabbit	3	0.1	Non irritating	Suberg, 1984b
5,000	Rabbit	6	0.1	Non irritating	Julou *et al*, 1973
12,500	Rabbit	N.D.	N.D.	Non irritating	Rowe *et al*, 1948
12,500	Rabbit	N.D.	0.7 - 1.0	Non irritating	Refojo *et al*, 1985
30,000	Rabbit	6	0.1	Non irritating	Julou *et al*, 1973
100,000	Rabbit	6	0.1	Non irritating	Julou *et al*, 1973
N.D.	Rabbit	6	0.1	Non irritating	Clark *et al*, 1979
N.D.	Rabbit	N.D.	0.1	Non irritating	Guillot *et al*, 1979

N.D. no data

8.2.4 Skin Sensitisation

The skin sensitisation potential of PDMS (350 cs) was evaluated in a preliminary study by Nosanchuk (1968). Six male Hartley guinea pigs received weekly injections of a 1:1 mixture of PDMS and Freunds complete Adjuvant (FCA). The initial injection of 0.5 ml was made into each heel pad (ie a total volume of 2.0 ml) and then given in weekly injections of 0.05 ml in each heel pad and 1.0 ml subcutaneously in the flank for three weeks. Subsequently, two additional four-dose courses were administered (1.0 ml weekly subcutaneous flank injections of a 3:1 PDMS-FCA mixture). Microscopic examination was made of lymph nodes, liver, spleen, lung and injection sites, taken at study termination. Granulomatous inflammation was observed at the injection sites and the popliteal lymph nodes were enlarged in all animals; this may have been due in part to the FCA. Moreover, in view of the large dosage administered (approximately 500 mg/kg body weight), a granulomatous reaction is to be expected. Despite the large quantities injected, no evidence of antibody production was found when pre-inoculation and serial post-inoculation sera were assayed for antibodies by passive cutaneous anaphylaxis and Ouchterlony gel diffusion. Immediate and delayed cutaneous hypersensitivity potential were assayed by injecting 0.001 l of PDMS (350 cs) intradermally into animals which had previously received PDMS via heel pad injection, and observing skin reactions at 20 mininutes and at 24, 48 and 72 hours. No effects were observed. On the basis of this, Nosanchuk (1968) concluded that PDMS displays no skin sensitisation potential.

Jackson (1979) evaluated the skin sensitisation potential of PDMS (unspecified viscosity) in a guinea pig. No details of the methods were provided, except that an induction dose of 10% w/w solution of PDMS in olive oil was applied followed by a challenge dose of 10%, 1% and 0.1% (w/w) in olive oil. No skin irritation or allergic response was observed. Furthermore, dermal sensitisation was not observed in mice following a challenge with polydimethylsiloxane (viscosity not specified) (US-EPA, 1992).

A preparation containing approximately 50 % PDMS (350 cs) was evaluated for skin sensitisation in the modified split adjuvant method (Hoffman, 1992). Five groups of guinea pigs (saline and alcohol controls, one positive control, one vehicle control and one experimental group) were used for this study. The groups were observed for skin irritation and sensitisation immediately prior to each induction dose and at 24, 48 and 72 hours following the challenge dose. No irritation was observed in any treatment group during the induction phase. Following challenge, no evidence of skin irritation or sensitisation was observed in any of the test or negative control groups. On the basis of these results, PDMS (350 cs) exhibited no potential to cause skin sensitisation in the guinea pig.

On the basis of these results, PDMS displays no evidence of cutaneous allergenic potential

8.3 SUBACUTE TOXICITY

Subacute toxicity studies using PDMS of varying viscosities demonstrated no significant adverse effects different routes of following administration for periods of up to 28 days to rats and mice; limited inhalational studies also showed no effect in cats, rabbits or guinea pigs.

Unless otherwise stated in subacute, subchronic and chronic studies on a commercially available antifoam, its composition can be regarded as a mixture of PDMS (1,000 cs) and silica in a ratio of 96:4.

Dietary doses reported in the literature as mg/kg or percentage in the food, have been converted in this report into mg/kg bw using standard conversion factors.

8.3.1 Oral

Subacute oral toxicity of PDMS has been evaluated by gavage and feeding studies. Rowe *et al* (1948) conducted a 28 day gavage study on PDMS (350 cs). Five groups of 5 rats received 1,000, 2,000, 5,000, 10,000 or 20,000 mg/kg bw, 5 days/week for 4 weeks. Controls received 4.0 ml of olive oil per day. Four deaths occurred during the study due to non-treatment related causes. The growth rate of remaining test animals was comparable with that of controls. No adverse effects were observed on haematological parameters, organ weights or histopathology. The No Observed Effect Level was thus greater than 20,000 mg/kg bw. These results on PDMS (350 cs) were also confirmed by a more limited study involving dietary administration (Union Carbide, 1978).

Bien and Buntrock (1974) studied the effects of PDMS (200 cs) alone and PDMS (1,000 cs) in combination with finely dispersed silica (no compositional data given but comparison with other commercially available antifoams suggests it was 96% PDMS and 4% silica) in a 28 day study in groups of 10 male rats. The two test groups received 9,800 mg/kg bw daily 5 days/week; the control group received an equal dose of liquid paraffin. Body weight gain was similar in the test and control groups. There was no evidence of any response or toxicological signs and no significant effect on spleen, heart, liver or kidney weights. Haematological studies conducted on blood samples taken after 2 and 4 weeks revealed no adverse effects.

A more extensive study evaluated the effect of PDMS (35, 350 and 1,000 cs) in a 28 day feeding study at 3 dietary levels providing daily doses of 500, 2,500 and 5,000 mg/kg bw (1%, 5% and 10%

in the food) in groups of 6 male and 6 female Sprague Dawley rats. Two groups of control animals received an untreated diet. The most notable difference between treatments was an increase in food consumption; this was particularly apparent with PDMS of 350 and 1,000 cs; it was not accompanied by any increase in body weights indicating that the added PDMS had no calorific value. No autopsies were conducted on surviving animals (Hoffman *et al*, 1987).

In a gavage study, Hobbs *et al* (1972) administered 50 cs PDMS to male Sprague Dawley rats and 350 cs PDMS to FDRL strain male rats at a single dose level of 3,200 mg/kg bw for either 7 (PDMS 50 cs) or 6 (PDMS 350 cs) successive days. Control animals received saline. Test and control groups contained 10 animals. No effects were observed on mortality index, general appearance or body weight gain. No adverse effects were observed at autopsy.

A parallel 28 day study was conducted in the mouse using PDMS (35 and 1,000 cs) at 3 dietary levels providing daily doses 1,500, 7,500 and 15,000 mg/kg bw (1%, 5% and 10% in the food) in groups of 6 male and 6 female mice (Hoffman *et al*, 1987). The two control groups received untreated diet. No significant signs of toxicity, changes in behaviour or mortality were observed. Although there was same correlation between the high dose groups and increased food consumption, there was no significant difference in mean body weight between test and control groups. Slight to severe anal leakage was observed in animals receiving the top dose, this was inversely correlated with the viscosity of the fluid. These findings have been confirmed in a similar experiment in rats using PDMS (35 cs) at dose levels of 1,500 and 5,000 mg/kg bw (3% and 10% in the food) in the diet (Hunter, 1987).

In summary, PDMS of various viscosities produces no adverse effects in rats or mice when administered orally over a period of several weeks.

8.3.2 Dermal

Bien and Buntrock (1974) studied the effects of dermal application of PDMS (200 cs and 1,000 cs) pure and in combination with finely dispersed silica (commercially available antifoam). Application of the test materials to rabbits ears (dose not specified) on the shaved dorsal skin of guinea pigs 5 days/week for 4 weeks had no effect either on skin irritation or toxicity.

A subacute dermal study on rabbits has been conducted to evaluate any potential effects on the male reproductive system (Hobbs *et al*, 1972). Ten percent of the body surface of adult male New Zealand rabbits was clipped 24 hours prior to applying (without rubbing) PDMS (50, 350 or 12,500 cs) at a dose rate of 200 mg/kg bw. There were 10 animals per group and 4 control

animals remained untreated. Applications were made daily for a total of 28 consecutive days. The sites remained uncovered but precautions were taken to prevent ingestion of the test substance. No effects were observed on mortality index, general appearance or body weight gain. There was no evidence of skin irritation. At terminal sacrifice, gross autopsy revealed no significant effects; testes weight and histopathological appearance were normal.

8.3.3 Inhalation

The subacute inhalation toxicity of PDMS (140 cs) was reported by Gloxhuber and Hecht (1955, 1956). One cat, rabbit and guinea pig, 2 rats and 4 mice were exposed for 4 h/d for 29 days to a dense aerosol; 10 ml was sprayed into a chamber of 400 l capacity giving an approximately nominal concentration of 23.7 mg/l. The authors reported that the mist quickly settled on the interior surfaces and fur of the animals; the possibility of ingestion of PDMS can therefore not be excluded. No particle size data or analytical measurements were recorded so there can be no certainty that significant amounts entered the respiratory system.

No effects were observed in the cat, rabbit, guinea pig or rats on body weight gain or results of blood and urinary analysis. All of the mice died, one during the course of exposure and the three others 1-3 weeks after the end of the study. No autopsy was performed but the authors concluded that the deaths were not associated with the treatment.

8.4 SUB CHRONIC TOXICITY

8.4.1 Oral

Where dietary doses were quoted in the literature as mg/kg or percentage in the food, there have been converted in this report to mg/kg bw (using standard conversion factors).

PDMS of 5 viscosities (50, 350, 1,000, 10,000 and 60,000 cs) was administered at 1% in the diet to Sprague-Dawley rats for 13 weeks (Deichman, 1957). Twenty animals per sex were utilised in the control and 10 animals per sex in the 5 test groups. No compound related alteration of weight gain, organ weight, clinical chemistry or histopathology was observed in this study.

This study was described in more detail by McDonald *et al* (1960). Only one dose level was used. Based on an accurate measurement of food consumption, the average daily intake of PDMS was 183 mg/rat, which equates to 730 mg/kg bw assuming a 250 g rat. Although body weight gain was slightly depressed in treated animals, due to the reduced nutritive value of the diet, no significant

histological changes were noted in spleen, kidneys, liver, testes or ovaries, uterus, aorta, stomach and small or large intestine.

PDMS of three viscosities (35, 350 and 1,000 cs) was administered in the food to groups of 20 male and 20 female Sprague-Dawley rats for 13 weeks at concentrations of 0, 500, 2,500 and 5,000 mg/kg bw (0, 10,000, 50,000 and 100,000 ppm in the food) (Hoffman *et al*, 1989). There were 2 control groups. No compound related deaths were observed. A significant increase in food consumption with no consistent difference in body weight, was observed in the 2,500 and 5,000 mg/kg bw group. This was considered to be due to compensation for the non-nutritive part of the food. Slight to moderate anal leakage was observed in all animals receiving 5,000 mg/kg bw and in those receiving 2,500 mg/kg bw, low viscosity PDMS diet. Mild chronic inflammation of the cornea was seen in the eyes of a few rats; mineralisation of the cornea was also present in some animals. These lesions were attributed by the author to direct ocular irritation from PDMS fluids in the food; they occurred in a non-dose related manner. Three lymphomas were seen in the treated males, two in rats receiving 500 mg/kg bw (1,000 cs fluid) and one in the 500 mg/kg bw (35 cs fluid) group. These were considered spontaneous neoplasms and not related to treatment because the incidence was unrelated to dose and was within historical control incidences. Nevertheless, as lymphomas in young rats are unusual, an additional study with a larger number of animals was conducted (Manston *et al* 1989). One hundred male rats were utilised in each of the 2 control groups and the 3 test groups. A single dose of 5,000 mg/kg bw (100,000 ppm in the food) of PDMS at each of the 3 viscosities (35, 350 and 1,000 cs) was administered in the diet. A significantly greater mean food consumption was observed in the test groups when compared to the control. This was considered to reflect compensation for the non-nutritive component of the diet. No significant changes of toxicological or biological significance were observed in the haematology, histopathology or necropsy evaluations. No lymphomas or corneal changes were observed.

PDMS (35 cs) was administered to CD-1 mice (20 animals/sex) for 13 weeks at dietary levels providing daily doses of 0, 7,500 and 15,000 mg/kg bw (0, 50,000 and 100,000 ppm in the food) (King and Siddiqui, 1989). No compound related death was observed. An increase in food consumption, without a consistent difference in body weight, was observed in the 15,000 mg/kg bw group and is considered to be due to compensation for the non-nutritive part of the food. Slight to moderate anal leakage occurred in animals treated with 15,000 mg/kg bw PDMS and a lesser degree of leakage in some animals treated with 7,500 mg/kg bw. No other differences were seen in clinical condition, organ weight or histopathological findings.

In a study by Child *et al* (1951) groups of 2 dogs received a daily dose of 0, 300, 1,000 or 3,000 mg/kg bw of a commercially available antifoam based on PDMS (1,000 cs) in their diet for 6

months. Chewing was observed after nearly every "antifoam meal" as well as ejection of moist and loose stools. No other adverse signs of toxicity or pathological findings were observed. In a similar feeding study by Carson *et al* (1966) PDMS (50 or 250 cs) was administered at 1% in the diet to rabbits and rats for 8 and 12 months respectively. PDMS (350 cs) was also fed to in both species in diets that contained 0.8% cholesterol. Two control groups (untreated diet and diet containing 0.8% cholesterol) were included. No significant differences were found between the groups receiving the polysiloxanes and those receiving the basal control diet on examination of growth, urinalysis, haematology or clinical chemistry, organ weight or tissue morphology.

8.4.2 Dermal

In a limited study (Gloxhuber and Hecht; 1955, 1956) applied PDMS (140 cs) to one ear of one rabbit (volume not quoted) once a day for 60 days. Comparison of the treated and untreated ears showed no evidence of irritation or other damage. In a second experiment, one ear of each of 3 rabbits was treated twice daily with PDMS (75 cs) for 60-100 treatments. No effect of treatment was observed and haematological findings were normal.

8.4.3 Inhalation

The 90 day inhalation toxicity of PDMS aerosols have been examined in two experiments. Groups of 3 rabbits per sex were used as controls and 5 animal per sex were used in each dose group. Formulation (1) consisted of PDMS (10 cs) (0.2%), absolute ethanol (29.8%), Freon 115 (35%) and Freon 12 (35%) (Industrial Biotest Lab., 1963a) and formulation (2) of PDMS (12,500 cs) (5%), Freon 115 (67.5%) and Freon 12 (27.5%) (Industrial Biotest Lab., 1963b); in both experiments, a 15 seconds aerosol burst was delivered into the exposure chamber and the experimental animals were exposed to the resulting concentration for a total of 15 minutes. Exposures were 2 times/day, 5 days/week. PDMS concentrations were not measured. No effect was seen on mortality, clinical symptoms, body weight gain, haematology and pathology.

8.4.4 Summary

There is no evidence that subchronic oral, dermal or inhalative administration of PDMS to rats, rabbits or dogs results in any significant adverse effects attributable to the test substance. There also appears to be no species difference in toxicity. The studies conducted during the 1950's and 1960's predate GLP and were conducted without reference to current day standards.

8.5 MUTAGENICITY

8.5.1 Gene Mutation in Bacteria: Ames Salmonella Test

PDMS of various viscosities (50, 100 and 1,000 cs) diluted in absolute ethanol were tested in *Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538 with and without activation by rat liver microsomal preparation (S9 liver homogenate) (Isquith and Whaley, 1978, 1979). No increase in revertants was observed. All positive controls were active and the solvent control gave negative results.

A PDMS emulsion (composition not specified), was included in a screen of 25 cosmetic ingredients (Blevins and Taylor, 1982). Reversion of *Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538 was examined with and without metabolic activation (S9 liver homogenate). Solvent negative controls and 4 positive controls were tested simultaneously. A spot test used for the initial screening showed that the PDMS emulsion yielded one positive result with strain TA 100. This was not considered significant in view of the high background counts observed with strain TA 100 in the presence of the solvent control, double distilled water. The PDMS emulsion clearly caused no increase in revertants in the other strains. A plate incorporation assay was then repeated at 3 dose levels, with and without S9 metabolic activation. Negative and positive controls were run simultaneously. No dose-related effect was observed and the number of revertant colonies with PDMS was the same with solvent in all strains. Therefore PDMS was considered not to induce gene mutation in bacteria.

8.5.2 Chromosome Aberration in Mammalian Cells in Vitro

PDMS of high viscosity was evaluated for clastogenic potential in an extensive comparative analysis conducted by Ishidate *et al* (1988) on 951 chemicals. The material was placed in contact with chinese hamster fibroblasts derived from lung tissue for 48 h; no metabolic activation system was used. Structural and numerical chromosome damage was evaluated by light microscopy. PDMS had no effect on chromosome aberration frequency.

8.6 CHRONIC TOXICITY AND CARCINOGENICITY

Where dietary doses quoted in the literature as mg/kg or percentage in the food, these have been converted in this report into mg/kg bw using standard conversion factors.

Rowe *et al* (1950) fed a group of 25 male and 25 female rats on a standard diet which provided daily 140 mg/kg bw (0.28% in the food) of a commercially available PDMS antifoam (PDMS 1,000 cs + silica). A similar group of 50 animals received an untreated diet. The mortality rate of control and test animals was high due to respiratory disease; the survival rate was 18.4 and 18.8% in the control and test groups, indicating that the deaths were not associated with treatment. Body weight gain was markedly increased in the males receiving the test substance; parallel changes were not seen in females. No appreciable differences were seen in heart, liver, kidney, spleen or testes weights between test and control animals. In view of the small number of animals remaining at termination, no meaningful conclusions can be drawn. No increase in tumour incidence was seen in the test animals. Mild fatty changes were apparent in the liver and kidney of test and control animals and are therefore not attributable to treatment. Total liver lipid content was comparable in both groups. In conclusion, Rowe *et al* (1950) found no evidence of chronic or carcinogenic effects in a 2 year feeding study of PDMS in rats. This is also supported by a limited study by Gloxhuber and Hecht (1955, 1956) in which 10 rats received a diet which provided daily 50 mg/kg bw (1,000 ppm in the food) PDMS (140 cs) emulsion for 112 weeks. No significant effect on body weight gain was observed. The most common cause of death was lung abscess; the authors did not consider this to be treatment related.

The chronic toxicity of a commercial antifoam was evaluated by Cutler *et al* (1974) in an 18 month study in an outlined strain of mice. Groups of male and female mice received diets providing daily 0 (control), 375 or 3,750 mg/kg bw (0, 0.23% and 2.35% in the food) of the test substance for 76 weeks from weaning (4-5 weeks of age). Another group of male and female mice (mean numbers = 45 animals) received at weaning a single subcutaneous injection of 0.2 ml of the test mixture (equivalent to 200 mg PDMS) or 0.2 ml of liquid paraffin (control animals). No significant increase in mortality was observed during the course of the feeding study. Body weight gain was not recorded. The study was terminated at 80 weeks of age. Macro and microscopic examination, revealed no significant increase in malignant or benign tumours in those animals which had received the test substance either in the diet or via subcutaneous injection. The only notable observation was significant decrease in subcutaneous fibromas in male mice given subcutaneous injection of PDMS as compared to liquid paraffin. The incidence of papillary adenomas of the lungs was reduced in male and female mice receiving PDMS in the diet. The only significant non-neoplastic change was an increase in superficial stomach ulcers in males in the low dose group and a significant decrease in uterine atrophy in females in the high dose group. Fifteen percent of males receiving the subcutaneous injection displayed an increased incidence of cysts at the injection site. In addition in this group, there was a significant reduction in the percentage of animals which displayed a proteinaceous plug in the urinary bladder. Tissue samples of liver,

kidney, spleen and perirenal fat of 5 mice which had received PDMS either in the diet or subcutaneously, were analysed for silicones; none were detected.

Calandra *et al* (1976) in a review of dietary studies reported that oral doses of 40 or 400 mg PDMS/kg bw for 2 years in rats or dogs did not result in any evidence of carcinogenicity (no details available).

Information on the chronic toxicity of PDMS (350 cs) in primates has been generated as part of a study on reproductive performance in four male Stumptailed Macaques (Calandra, 1968). Dermal application of 2,000 mg/kg bw were made 5 times a week for 26 months; 4 control animals received no treatment. Food consumption and body weight gain during the course of the study were found to be normal. No behavioural changes were noted. Haematology, clinical chemistry and urinalysis conducted during the 7th and 20th month of the study revealed no abnormal effects of treatment. Thirty-nine months after dosing commenced, the animals were killed. Gross and microscopic examination of tissues revealed no abnormal effects.

In summary, the results in rats, dogs and monkeys support the conclusion that PDMS is not carcinogenic in laboratory animals following prolonged administration in the diet. No other significant adverse effects were observed. These studies were conducted prior to 1980 and the study protocols would not conform to modern day standards.

8.7 DEVELOPMENTAL AND REPRODUCTIVE TOXICITY

8.7.1 Teratogenicity

The most comprehensive studies on the teratogenic potential of PDMS have been conducted using 350 cs fluid in rabbits and rats (Kennedy *et al*, 1976).

Groups of 15 pregnant New Zealand rabbits were dosed from gestation day 6 to 18 by subcutaneous injection to ensure sufficient absorption of the test material, although it is not a physiological route of exposure. The dose levels were as follows:

Low dose: 20 mg/kg bw PDMS (1:50 in sesame oil)

Intermediate: 200 mg/kg bw PDMS (1:5 in sesame oil)

High dose: 1,000 mg/kg bw PDMS (undiluted)

Three control groups received sesame oil injected subcutaneously at dose levels of 20, 200 or 1,000 mg/kg bw. Additionally two other groups of rabbits were exposed dermally on gestation days 6 to 18 to 200 mg/kg bw PDMS (350 cs) diluted with corn oil or sesame oil. The control groups (10 animals) received 1 mg/kg corn oil or 200 mg/kg bw sesame oil, applied dermally. In both studies the dams were killed on day 29 and the litters delivered by Caesarean section. The uteri were examined for numbers of implantation and resorption sites and the number and weight of live and dead foetuses was recorded. Inspections were made for gross and skeletal abnormalities.

No effects were observed on maternal body weight from either dermal or subcutaneous injection. An increase in resorption sites was observed, the incidence being in direct proportion to the amount of material administered. This was apparent with both the test and control groups and particularly with the subcutaneous route. No foetal abnormalities were observed at the top dose level. An increase in soft tissue abnormalities, principally umbilical hernia and clubbing of the feet, was observed at 200 mg/kg bw. Similar findings were observed with dermal exposure, where 3.8% of the foetuses displayed gross abnormalities. Two foetuses showed both synophthalmia and umbilical hernia and one displayed clubbing of the extremities. Skeletal examination revealed 2 foetuses with frontal skull deformities (Kennedy *et al*, 1976).

In view of the results, a more detailed study was conducted, on rats and rabbits.

Groups of approximately 20 female pregnant FDRL rats were dosed from gestation day 6 to 16 by subcutaneous injection with either 20, 200 or 1,000 mg/kg bw PDMS (350 cs) in sesame oil. On day 20, the dams were killed and examined for implantation sites, number and weight of live and dead foetuses and number of resorption sites. Inspections were made for gross and skeletal abnormalities. No compound-related gross pathological effects or changes in reproductive performance were seen in the dams. The mean number of implant sites and viable pups of treated animals were slightly but not significantly lower than in the control. Body weight of treated pups was normal and no gross abnormalities were observed. Skeletal examination revealed a slight increase in the number of foetuses with incompletely developed sternebrae born to dams receiving 1,000 mg/kg bw PDMS. In addition, this group displayed a slightly greater incidence of incomplete closure of the cranial bones. These effects are attributable to delayed ossification (Kennedy *et al*, 1976).

In the parallel study, groups of 15 pregnant New Zealand rabbits were dosed from gestation day 6 to 18 by subcutaneous injection with 20, 200 or 1,000 mg/kg bw PDMS (350 cs) in sesame seed oil; the control group received 1,000 mg/kg bw sesame oil. On day 29, the dams were killed and the litters delivered by Caesarean section. The number of implantation and resorption sites,

number and weight of live and dead foetuses was recorded. Inspections were made for gross and skeletal abnormalities. Two animals from the intermediate and high dose group died during pregnancy. The mean number of implant sites per dam in the control, mid and high dose groups were comparable; the slightly lower number of implantations observed in the low dosage groups is not considered to be significant. The number of resorptions and *in utero* mortality were slightly greater in the treated animals than the controls but these findings were not dose related and were within expected limits of variation. No effect of treatment on foetal weight was observed. There were no marked skeletal abnormalities apart from slight variations in the number of ribs. Due to poor quality of the data, no definitive conclusion on the teratogenic potential of PDMS can be made (Kennedy *et al*, 1976).

In a more recent study, Bates *et al* (1985) evaluated the effect of PDMS (350 cs) on foetal development in the rat (strain not specified). The fluid was injected subcutaneously along the spine of pregnant females. In a preliminary, range finding study, toxicity was evaluated with two different dosing procedures (A and B) at cumulative dose levels of 5,000, 10,000 and 20,000 mg/kg bw PDMS. Control animals received carboxymethylcellulose or 0.85% saline (dose not specified). Group sizes were not specified. Animals in Group A received 10% of the total cumulative dose on each of gestation days 6-15 inclusive. Animals in Group B received the total cumulative dose seven days prior to mating. The only effect observed was a significant post-implantation loss in the 5,000 and 10,000 mg/kg bw PDMS dose groups which had been injected prior to mating. In order to ensure that there was evidence of toxicity in the definitive assay the pre-dosing procedure (B) was adopted. Dams were injected 7 days prior to mating with 1,000, 10,000 or 20,000 mg/kg bw PDMS; control animals received 0.85% saline. No clinical signs of toxicity were evident in the dams. Gross, visceral and skeletal examination of the foetuses showed no significant effects. There were no signs of foetotoxicity but the ratio of female/male pups was significantly increased in the intermediate dose group as compared to the control. In view of the absence of any similar effect in the high dose group, this was considered to be of no biological significance. The authors concluded that under the conditions of this test, PDMS 350 cs displayed no teratogenic potential.

The only other viscosity of PDMS to be tested was 10 cs (Jackson, 1966). Pregnant New Zealand rabbits (10 animals per groups) received either 200 mg/kg bw PDMS (10 cs), or 200 mg/kg bw corn oil by dermal application on gestation days 6 to 19. A third group was included as untreated controls. No signs of maternal toxicity or effects on maternal body weight were observed. On day 19, the dams were killed and the litters delivered by Caesarian section. A slight increase in resorption sites in the PDMS treated group (8.2% versus 3-4% for the corn oil control group) was observed. Only 3 of 10 females exhibited one or more resorption sites and this value (30%) is within the expected range for this strain of rabbit. Inspection of the foetuses for gross and skeletal

abnormalities revealed that 98.7% of the offspring from PDMS-treated dams were normal; one foetus displayed clubbing of the extremities (*talipes varus*). Umbilical hernias occurred in one foetus in each of the control groups. It was concluded that PDMS (10 cs) displays no evidence of teratogenic effects in the rabbit.

In conclusion, PDMS (350 cs) displayed no clear evidence of teratogenic effects even when injected at high levels into rats or rabbits. The absence of absorption of PDMS from the diet (see Section 7) strongly supports the conclusion that PDMS is unlikely to present teratogenic risk by oral administration. PDMS (10 cs) caused no teratogenic effects in the rabbit.

8.7.2 Reproductive performance

Reproductive performance in rats was also investigated at IBT (Kennedy *et al,* 1976). To evaluate effects on fertility and gestation, male and female rats received subcutaneous injections of 20 or 200 mg/kg bw PDMS (350 cs) or 200 mg/kg bw sesame oil. Groups of about 10 males were dosed 3 times per week for 10 weeks prior to mating. Groups of 30 female rats were dosed 7 days/week for 2 weeks prior to mating. Dosing was continued until pregnancy was confirmed. On day 13 of gestation, Caesarean section was carried out on 50% of the dams. The number of implant sites and dead pups were counted and examined. The number of viable foetuses in treated rats slightly exceeded that in controls. There was no evidence of any foetal deaths or abnormalities in test groups and the incidence of resorptions was also not effected by treatment. The remaining females were permitted to carry the litters to term and dosing continued for 21 days during lactation, during which time periodic inspections and weighings were made. The survival rate of the pups between birth and 4 days was similar in test and control animals. No abnormal patterns of behaviour were observed in the dams or the pups. At 21 days no gross abnormalities were observed in dams and pups.

To evaluate *peri-* and *post*-natal development, 4 groups of 20 adult female rats that had previously borne live litters, were mated. From day 15 of gestation and during lactation, the animals were dosed daily with 20, 200 or 1,000 mg/kg bw PDMS (350 cs) or 1,000 mg/kg bw sesame oil by subcutaneous injection. The number of live and dead pups were counted at birth and at 4 days and 21 days of age. Body weight was measured at birth and 21 days. Gestation, viability and lactation indices were calculated from these measurements; no differences between test and control groups were observed. No treatment-related deaths occurred in the dams. Two litters in the high dose level groups were born dead and there was a greater *in utero* mortality among the animals of the intermediate and high dose groups. However, both the average body weight and number of viable pups per litter were not effected.

Studies were also conducted on the effects of PDMS (350 cs) on the reproductive performance of primates (Calandra, 1968). The dorsal area of four adult male Stumptailed Macaques was shaved and the test substance was applied at a dose rate of 2,000 mg/kg bw, 5 times per week for 26 months before mating with receptive females. Four control animals received no treatment. Food consumption and body weight gain during the course of the study were found to be normal. Haematology, clinical chemistry and urinalyses conducted during the 7th and 20th month of the study revealed no abnormal effects of treatment. Analysis of semen during months 14, 15 and 24 revealed no effect on sperm number or motility. Testicular biopsy during months 8 and 12 revealed no abnormalities in the development of the testes or maturation of the sperm as revealed by light microscopy. All of the test animals and two of the control animals were successfully bred with control females. All pregnancies were allowed to go to term and produced viable offspring. No gross abnormalities were observed. The animals were weaned and during the month 39 of the study, all adult males and infants were killed. Microscopic examination of heart, lung, liver, oesophages, testis, salivary gland, kidney, stomach and bladder revealed also abnormal effects.

In conclusion, PDMS (350 cs) administered subcutaneously to male and female rats prior to mating had no effect on fertility or gestation. It had slight effects on *peri* and *post*natal development at the highest dose levels but the contribution of the stress of the high doses given to this response is not clear. Dermal application to male monkeys had no effect on male reproductive performance.

8.8 SPECIAL STUDIES

8.8.1 Immunotoxicity

PDMS (1,000 cs) fluid has been evaluated in a *Listeria* host resistance assay (Klykken *et al*, 1991a). Three Groups of 10 female B6C3F1 mice received 1 ml of PDMS or saline by subcutaneous injection into the mid back. After 10, 45 and 90 days respectively the animals were challenged with 0.2 ml *Listeria* via an intravenous injection. Range finding LD50 determinations were performed prior to the main study to determine the number of *Listeria* to inject per animal. All operations were carried out aseptically. System validation was achieved at each exposure period by exposing groups of matched non-PDMS treated mice to the immuno-suppressive (cyclophosphamide, 200 mg/kg bw) and immuno-enhancing agents (*Corynebacterium parum*, 35 mg/kg bw) respectively. Potential effects on immune competence were evaluated by comparing life span and mortality data from PDMS and saline control mice. Irrespective of whether the data sets were evaluated separately or collated over the three exposure periods, no treatment related effects were evident. Under the conditions of this assay it is concluded that PDMS displays no effect on immune competence.

An additional experiment (Klykken *et al*, 1991b) was conducted to evaluate whether PDMS can stimulate an immunological response and initiate a T lymphocyte mediated immune granulomatous reaction. Evidence of immunological sensitisation was examined in T cell deficient nude mice (nu/nu) and their immunologically normal heterozygote litter mates (nu/+). To maintain aseptic conditions, injection sites were shaved, swabbed with PVP iodine and 70% ethanol and, after injection, a thin film of flexible collodion USP was applied. Groups of 10 nu/nu or nu/+ mice received subcutaneous injection of either 0.1 ml PDMS (1,000 cs) or 0.1 ml of PDMS plus 0.1 ml Freund's complete Adjuvant (FCA) in the dorsal thoracic region. A second injection of 0.2 ml PDMS alone, was made in the abdominal region. Twenty-eight days later the animals were observed for 2, 6 or 13 weeks after which they were killed. At this stage, the abdominal injection site and surrounding tissues were processed for histological evaluation. No differences were observed at any of the time points between the test groups in terms of cellularity or propositions of neutrophils, macrophages, giant cells, lymphocytes, plasma and epitheloid cells, basophils and eosinophils. This data support the conclusion that injection of PDMS does not stimulate an immunological response.

8.8.2 Cytotoxicity

PDMS (10 cs to 1,000 cs) were evaluated for cytotoxic effect by placing the material in direct contact with a confluent monolayer of human embryonic cells (Isquith and Miller, 1984). Each cell culture was examined microscopically to determine suitability for use in the assay and a sterile Millipore (R) filter pad saturated with test material was placed in direct contact with the cell monolayer. After 24 hours incubation, the cytotoxic effect was evaluated microscopically against both positive and negative controls run simultaneously. No cytotoxic effect was produced by any of the PDMS.

SECTION 9. EFFECTS ON MAN

9.1 CONTINUAL APPLICATION OF A CREAM TO HUMAN SKIN

Where workers are exposed to substances which are hazardous to the skin, it is important to evaluate the protection offered by skin protection creams. The efficacy of a silicone-bentonite mixture was demonstrated in a study by Suskind (1954). Workers exposed periodically or continually to skin irritants, sensitisers and defatting materials applied a thin film of a cream (52.5% PDMS, (350 cs) in a bentonite base) on exposed skin surfaces for periods of 2 to 8 months. The formulation appeared to have a considerable clinical protective value against most of the chemical agents and even when applied regularly for 5 to 8 months, the cream itself produced no irritation or hypersensitivity reactions.

9.2 DERMAL ABSORPTION

Absorption of PDMS (100 cs) was evaluated by applying it to the back of 5 men (23 to 29 years old), daily for 10 days at a dose level of 50 mg/kg bw. The material was evenly distributed over the entire surface of the back and remained in contact with the skin for a period of 20 hours after which time any excess materials was washed off. PDMS absorption was determined by analysis for elemental silicon in blood and urine. Baseline levels were determined prior to administration. Silicon was analysed by optical emission spectroscopy; this is not the most appropriate technique as interference from other elements should not be excluded. Sample preparation consisted of dilution of the biological fluids with an aqueous solution of germanium dioxide which served as an internal standard. Individual daily diets were recorded and drinking water and representative brands of beers were monitored for silicone content. Despite the possible interferences of other endogenous metal traces, no statistically significant increase of urinary or blood silicon levels were seen. There was no evidence of dermal absorption (Industrial Biotest Lab., 1968).

9.3 EFFECTS ON GLUCOSE ABSORPTION

The ability of PDMS to interfere with the gastrointestinal absorption of nutrients was evaluated by use of the glucose tolerance test (Reuse, 1979). Eight healthy, non-diabetic volunteers (19 to 26 years old, of both sexes) were submitted to the test. No participant was receiving medicaments at the time. After an overnight fast, the double-blind test was conducted in the morning; half of the volunteers ingested control preparation and the others a PDMS emulsion (15 mg/kg bw). Twenty minutes later 50 g glucose, dissolved in water was taken orally. Blood was taken from an

indwelling catheter in a fore-arm vein into heparinised tubes at 0, 30, 60, 90 and 120 minutes after taking the glucose.

Blood glucose was determined by the glucose oxidase method. The double blind study had a cross-over design, the procedure being repeated and reversed a week later. PDMS failed to modify the results of the glucose tolerance test. The basal level of glucose was similar in the two groups and the administration of the glucose induced in both groups a similar increase of blood glucose, peaking after 60 minutes.

This study indicates that PDMS does not interfere with oral glucose absorption under these conditions in man and therefore suggests that PDMS may not interfere with gastrointestinal absorption of nutrients or other essential dietary compounds.

9.4 SUMMARY

No adverse effects have been observed in man following the use of PDMS for many years in a large number of consumer applications involving frequent dermal (e.g. cosmetics) or oral (food additive) exposure.

SECTION 10. FIRST AID AND SAFE HANDLING ADVICE

First Aid

PDMS are known to be non hazardous to man and no special safety measures are required under normal operating conditions. The following first aid measures are only recommended in case of contact with the substance in unusually by large amounts.

Eye contact: Flush eyes with plenty of water, seek medical advice if irritation occurs.

Skin contact: Remove product mechanically by wiping with absorbent textile or paper, then wash with soap and water.

Ingestion: If large volumes are swallowed seek medical advice.

Safe Handling

Personal protection: Safety glasses

Technical protection: During storage no special measures required. PDMS fluids may become electrostatically charged during filling and transferring operations; equipment should be grounded.

Fire Fighting

In cases of a fire, all standard extinguishing media may be used.

Management of Spillage and Waste

Take up small spills with absorbent materials (e.g. sawdust, sand). Large spills should be contained with bunds and pumped into containers.

Disposal

For used PDMS fluids from non-dispersive industrial applications recycling/reclamation should be considered. If material recycling/reclamation is not feasible (e.g. small volumes, heavily

contaminated PDMS) the waste should be incinerated for energy recovery at a chemical waste incinerator or other licensed premises. PDMS from industrial sources should not be landfilled or discharged to drain.

BIBLIOGRAPHY

Anderson C, Hochgeschwender K, Weidemann H and Wilmes R, 1987. Studies of the oxidative photoinduced degradation of silicones in the aquatic environment. Chemosphere 16, 2567-2577.

Anliker R, Moser P and Poppinger D, 1988. Bioaccumulation of dyestuffs and organic pigments in fish. Relationships to hydrophobicity and steric factors. Chemosphere 17, 8, 1631-1644.

Annelin RB, 1979. Bioaccumulation of DC 561 transfer fluid in bullheads. DC Report I-0005-0669 cited in Reports and Studies n° 29 IMO/FAO/UNESCO/WMO/WHO/IAEA/UN/UNEP joint group of experts on the scientific aspect of marine pollution-GESAMP.

Annelin RB, 1991. Analysis of organosoluble silicon in peat bog litter from northeastern Ontario (Canada). DC international report No. 1991-10 000-36116, 8 March 1991. Dow Corning Corp., Midland, Michigan, USA.

Annelin RB and Frye CL, 1989. The piscine bioconcentration characteristics of cyclic and linear oligomeric permethylsiloxanes. Sci. Total Environ 83, 1-11.

Annelin RB, Galbraith TW and Siddiqui WH, 1989. Single and repeated dose pharmacokinetic studies of polydimethylsiloxanes in the rat. DC Technical Report No.1989-I0005-2581. Dow Corning Corp., Midland, Michigan, USA.

Annelin RB, Klein R and Varaprath S, 1994. Acute Toxicity of the Water Accommodated and Water Soluble Fractions of Dow Corning 50 cs PDMS Fluid with *Daphnia magna*. DC Internal Report 1994-I0000. Dow Corning Inc., Midland, Michigan, USA.

Ascon-Carbera M and Lebeault JM, 1993. Selection of xenobiotic degrading microorganisms in a biphasic aqueous-organic system. Appl. Environ. Microbiol. 59, 1717-1724.

Atkinson R, 1991. Kinetics of the gas-phase reactions of a series of organosilicon compounds with OH and NO_3 radicals at 297 ± 2 K. Environ. Sci. Technol. 25, 863-866.

ATS (1985). Organosiloxanes in fresh water and salt water sediments. Report to Silicones Health Council, 17 July 1985. Ann Arbor Technical Services. Michigan, USA

Aubert M, Aubert J, Augier H and Guillemaut C, 1985. Study of the toxicity of some silicone compounds in relation to marine biological chains. Chemosphere 14, 127-138.

Badinand MA, 1952. Etude Toxicologique de Quelques Dérivés Organiques du Silicium (Silicates, Siloxanes, Silicones). Bull. Soc. Pharm. Bordeaux 90 298-306.

Badura R, Buczek A and Kotz J, 1968. Investigations into the intravenous application of silicone oils (in dogs). Medycyna Weterynaryjna, 24 151-154.

Bates H, Filler R and Kimmel C, 1985. Developmental toxicity study of polydimethylsiloxane injection in the rat. Teratology, 31, 50A.

Batley GE and Hayes JW, 1991. Polyorganosiloxanes (silicones) in the aquatic environment of the Sidney region. Aust. J. Mar. Freshwater Res. 42, 287-293.

Battelle, 1992a. Fate and effects of PDMS : Soil amendment sludge disposal. Report to Dow Corning Corporation, Battelle Study No SC 900090. May 8, 1992. Battelle, Columbus Lab., Ohio, USA.

Battelle, 1992b. Fate and effects of PDMS : determination of PDMS degradation potential. Report to Dow Corning Corporation, Battelle Study No SC 900091. May 28, 1992.

Belt GH, King JG and Haupt HF, 1977. Augmenting summer stream flow by use of silicone antitranspirant. Cited by West KF, 1992. Water Resource Research, 13, 267-272.

Bien E and Buntrock P, 1974. Pharmakologish-toxicologische Untersuchungen von Silicon produkten. Pharmazie, 29, 530-534.

Blevins RD and Taylor DE, 1982. Mutagenicity screening of twenty-five cosmetic ingredients with Salmonella/microsome test. J. Environ. Sci. Health, A 17, 217.

Bomhard E, 1983. Baysilicone M 1000. Untersuchungen zur acute, oralen Toxizität an Maennlichen und Weiblichen Wistar Ratten. Internal Report, Bayer AG, Leverkusen, Germany.

Bruggeman A, Weber-Fung D, Opperhuizen A, Van der Steen J, Wijbenga A and Hutzinger O, 1984. Absorption and Retention of Polydimethylsiloxanes (Silicones) in Fish: Preliminary Experiments. Toxicol. Environ. Chem., 7, 287-296.

Buch RR and Ingebrigtson DN, 1979. Rearrangement of polydimethylsiloxane fluids on soil. Environ. Sci. Technol. 13, 676-679.

Buch RR, Lane TH, Annelin RB, Frye RB and Frye CL, 1984. Photolytic oxydative demethylation of aqueous dimethylsiloxanes. Environ. Toxicol. Chem. 3, 215-222.

Cabridenc R, 1978. Polydimethylsiloxanes, IRNS. Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicone Compounds on the Aquatic Environment. TNO, The Hague, The Netherlands.

Calandra JC, 1968. Dermal toxicity of PDMS/350 cs with regard to the reproductive capability of the primate. Industrial Bio Test Laboratories Inc. to DC Technical Report No. 1968-I0065-1059-12. Dow Corning Corp., Midland, Michigan, USA.

Calandra JC, 1976. Skin Contact Irritation Test with 200 Fluid/10 cs Industrial Bio Test Laboratories Inc. DC Technical Report No. 1976-I0065-1056-07. Dow Corning Corp., Midland, Michigan, USA.

Calandra JC, Keplinger ML, Hobbs EJ and Tyler LJ 1976. Health and environmental aspects of Polydimethylsiloxane fluids. Am. Chem. Soc. Polymer
Preprints 17 12.

Calandra JC, Keplinger ML, Hobbs EJ and Tyler LJ, 1976. Health and environmental aspects of Polydimethylsiloxane fluids. Polym. Prep., Am. Chem. Soc., Div. Polym. Chem. 17(1), 12-16.

Carpenter JC, Cella JA, Deron SB and Skelly-Frame EM, (1994). A study of the degradation of polydimethylsilocanes on soil. Submitted for publication to Chemosphere.

Carson S, Weinberg MS and Oser BL (1966). Safety evaluation of Dow Corning 360 fluid and antifoam A. The Toilet Goods Association No 45, 9-19.

Chenoweth MB, Holmes RE and Stark FO, 1956. The Physiological Assimilation of Dow Corning 200 Fluid. DC Technical Report No. 1956-I0065-1170-03. Dow Corning Corp., Midland, Michigan, USA.

Child GP, Paquin HO and Deichmann WB, 1951. Chronic toxicity of the Methylpolysiloxane ."DC Antifoam A" in dogs. Arch. Ind. Hyg., 3; p 479-482.

Clark LC and Gollan F, 1966. Survival of mamals breathing organic liquids equilibrated with oxygen at atmospheric pressure. Science 152, 1755-1756.

Clark CR, Marshall TC, Merickel BS, Sanchex A, Brownstein DG and Hobbs CH (1979). Toxicological Assessment of Heat Transfer Fluids Proposed for Use in Solar Energy Applications. Toxic. Appl. Pharmac. 51, 529-535.

Craig NCD and Caunter JE, 1990. The effects of Polydimethylsiloxane (PDMS) in sediment on the polychaete worm *Nereis diversicolor*. Chemosphere 21, 751-759.

Crompton TR, 1989. Analysis of organosilicon compounds, chapter 6. The Chemistry of Organic Silicon Compounds. Ed. S. Patai and Z. Rappoport, John Wiley & Sons Ltd.

Cutler MG, Collings AJ, Kiss IS and Sharratt M, 1974. A lifespan study of a polydimethylsiloxane in the mouse. Fd. Cosmet. Toxicol., 12, 443-450.

Deichmann B, 1957. Report on five silicone materials. DC report, 1006 5-1063 3. Dow Corning Corp., Midland, Michigan, USA.

Dive D, 1981. Etude comparée de la toxicité du PDMS et d'un PCB sur des protozoaires. Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicon Compouns on the Aquatic Environment. TNO, The Hague, The Netherlands.

Eales GJ and Taylor D, 1983. A study of the movement of a polydimethylsiloxane fluid in sediment columns-Phase 2. Dow Corning Report I-9039-002.

EAJ, 1981a. Chemical assessment annual report, 1981 edition : Chemicals in the environment. E.A. Off. Health Studies Report Series N°7. Environmental Agency of Japan.

EAJ, 1981b. Analysis of Silicone in edible Parts of Goby and Dace in Tokyo Area. EA Off Health Studies Report Series No. 7. Environ. Agency of Japan.

FAO/WHO, 1974 Expert Committee on Food Additives, World Health Org. Tech. Report Series 557, 18th Report, FAO Nutrition Meetings Report Series 54.

Firmin R, 1984. Les composés organosiliciés et l'environnement aquatique. Mémoire, Sciences Environnement, Université Libre Bruxelles. Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicon Compouns on the Aquatic Environment. TNO, The Hague, The Netherlands.

Fitzgerald JB and Mallette WG, 1960. The physiological effects of intravascular Antifoam A. School of Aviation Medicine. USAF Aerospace Medical Centre (ATC), Brooks Air Force Base, Texas.

Frye CL, 1987. A cautionary note concerning organosilicon analytical artifacts. Environ. Toxicol. Chem. 6, 329-330.

Frye CL, 1988. The environmental fate and ecological impact of organosilicon materials: a review. Sci. Total Environ. 73, 17-22.

Frye CL and Chu HK, 1988. The case against Mercury (II) methylation by aquatic environmental methysiloxanes. Environ. Toxicol. Chem. 7, 95-98.

Garrido L, Pfleider B, Papisov M and Ackerman JL, 1993. *In vivo* degradation of silicones. Magn. Reson. Med. 29/6, 839-843.

Gettings RL and Lane TH, 1982. The use of microecosystems in determining the environmental fate of polydimethylsiloxanes. DC. International Report 10005-10957, cited in Reports and Studies n° 29 IMO/FAO/UNESCO/WMO/WHO/IAE/UN/UNEP joint group of experts on the scientific aspects of marine pollution-GESAMP.

Gilliard Ch, 1980. Influence du DB 31 Dow Corning sur la respiration des boues activées dans l'épuration aérobie. Université Libre Bruxelles, Service Traitement des Eaux et Pollution. Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicone Compounds on the Aquatic Environment. TNO, The Hague, The Netherlands.

Gloxhuber C and Hecht G, 1955. Pharmakologische Untersuchungen an Siliconen. Arzneim-Forsch 5, 3-12.

Gloxhuber C and Hecht G, 1956. Pharmakologische Untersuchungen an Siliconen. Therapeutische Berichte 28, 44-47.

Gonnet JF and Guillot JP, 1985. Tests de Tolérance Locale chez le Lapin. Hazleton Report N° 505425. Rhone Poulenc, France.

Guillemaut C, Aubert J and Augier H, 1987. Recherche sur la contamination et la toxicité des organo-silicones vis-à-vis de la biomasse marine. Rev. Int. Océanogr. Méd. 85/86, 88-93.

Guillot JP, Giauffret JY and Martini MC, 1979. A study of skin and eye irritation in the rabbit due to different sources of some cosmetic raw materials. Part II Int. J. Cosmet. Sci. 1 (1), 27-57.

Harzdorf C, 1993. Analysis of PDMS in soil. Report to Centre Européen de Silicone (CES) Brussels. 28 July 1993, Belgium.

Henrich R.T. and McMahon JM , 1990a. USP Class V Extractables Study on PDMS. DC Technical Report No. 1990- I0000-35514. Dow Corning Corp., Midland, Michigan, USA.

Henrich RT and McMahon JM, 1990b. USP Class V Extractables Study of PDMS. DC Technical Report No. 1990- I0065-6835-01. Dow Corning Corp., Midland, Michigan, USA.

Hill RW, 1980a. Determination of acute toxicity of DC 561 and DC X2-3168 to mussel (*Mytilus edulis*), report DC 19039 (6 and 8). Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicone Compounds on the Aquatic Environment. TNO, The Hague, The Netherlands.

Hill RW, Caunter JE and Eales GJ, 1980b. Determination of the effect of spillage of Dow Corning fluid on the plaice (*Pleuronectes platessa*) in a static bioassay. ICI Brixham, report nr BL/B/2061.

Hill RW, Caunter JE and Eales GJ, 1984. Effect of an organosilicon formulation on embryos and larvae of sheepshead minnow (*Cyprinodon variegatus*). ICI Brixham report nr BL/B/2392. Cited in TNO Report to EEC No U/83/208(605) Evaluation of the Impact of Organo Silicon Compouns on the Aquatic Environment. TNO, The Hague, The Netherlands.

Hobbs EJ, Fancher OE and Calandra JC, 1972. Effect of selected organopolysiloxanes on male rat and rabbit reproductive organs. Toxicology and Applied Pharm. 21, p 45-54.

Hobbs EJ, Keplinger ML and Calandra JC, 1975. Toxicity of Polydimethylsiloxanes in certain environmental systems. Environ. Res. 10, 397-406

Hoffman RD, 1992. A skin sensitisation study of a 53% PDMS formulation in Guinea Pigs. Dow Corning Technical Report No. 1992-I0000-37079. Dow Corning Corp., Midland, Michigan, USA.

Hoffman RD, Stanton E, Hobbs EB, Kolesar GB and King DW, 1987. Palatability Studies of polydimethylsiloxanes in the rat when mixed with rodent diet. DC Technical Report No. 1987-I0005-1625. Dow Corning Corp., Midland, Michigan, USA.

Hoffman RD, Siddiqui WH, Zimmer MA, 1989. 90 day Subchronic Oral Toxicity Study with Polydimethylsiloxane in rats. DC Technical Report, No 1989-I0005-2563. Dow Corning Corp., Midland, Michigan, USA.

Houvenaghel GT, 1980. The study of the fate and impact of Polydimethylsiloxane introduced into the aquatic environment. Report I 9039-0002. Université Libre de Bruxelles, Belgium.

Howard PH, Durkin PR and Hanchett A, 1974. Environmental hazard assessment of liquid siloxanes. Syracuse University Research Corp. Report to EPA. EPA-560/2-75-004.

Hunter C, 1987. Anal leakage study of PDMS 35 cs in the diets of rats, DC Technical Report No. 1987, I0030-6131. Dow Corning Corp., Midland, Michigan, USA.

Industial Biotest Lab., 1963a. Report to Dow Corning Corporation: 90-day subacute aerosol inhalation toxicity of PDMS formulation 1. DC Technical Report No. 1963-10065-1056-01. Dow Corning Inc., Midland, Michigan, USA.

Industial Biotest Lab., 1963b. Report to Dow Corning Corporation: 90-day subacute aerosol inhalation toxicity of PDMS formulation 2. DC Technical Report No. 1963-10065-1062-02. Dow Corning Inc., Midland, Michigan, USA.

Industrial Biotest Lab., 1964. Report to Dow Corning Corporation: Skin Irritation Studies on two materials. PDMS 350 cs and DC X Fluid. Technical Report No. 1964-I0065-1069-02. Dow Corning Corp., Midland, Michigan, USA.

Industrial Biotest Lab., 1967. Report to Dow Corning Corporation: Range finding Eye Irriation Test on DC 200/350 cs. DC Technical Report No. 1967-I0065-1059-06. Dow Corning Corp., Midland, Michigan, USA.

Industrial Biotest Lab. Inc., 1968. Report to Dow Corning Corporation. Study of the absorption of Dow Corning 200/100 cs lot 6872 following dermal application to humans. DC Technical Report No. 1968-I0065-1057-04. Dow Corning Corp., Midland, Michigan, USA.

Isquith AJ and Miller BJ, 1984. Tissue Cell Biocompatibility of Dow Corning 200 Fluid:
10 cs: DC Report 1984-I0005-1201
20 cs: DC Report 1984-I0005-1202
50 cs: DC Report 1984-I0005-1203
100 cs: DC Report 1984-I0065-1057-12
350 cs: DC Report 1984-I0005-1197
500 cs: DC Report 1984-I0065-1198
1000 cs: DC Report 1984-I0065-1061-04.
Dow Corning Corp., Midland, Michigan, USA.

Isquith AJ and Whaley DP, 1978. Mutagenicity evaluation of Dow Corning 200 Fluid in the Ames bacterial assay. DC Report 1978-I0065-1063-16. Dow Corning Corp., Midland, Michigan, USA.

Isquith AJ and Whaley DP, 1979. Mutagenicity evaluation of Dow Corning 200 Fluid in the Ames bacterial assay. DC Report 1979-I0065-1063-17. Dow Corning Corp., Midland, Michigan, USA.

Ishidate MJr, Harmois MC and Sofuni, T, 1988. A comparative analysis of data on the clastogenicity of 951 chemical substances tested in mammalian cell cultures. Mutation Res., 195, 151.

Jackson GL, 1966. Report to DC Corporation. Rabbit Teratogenic Study DC 225 Fluid (10 cs PDMS). Industrial Biotest Laboratories. DC Technical Report No. 1966-I0065-1056-02. Dow Corning, Corp., Midland, Michigan, USA.

Jackson SJ, 1979. Silicone EP 6500. Acute oral toxicity, skin and eye irritation and skin sensitisation studies. ICI Report No. CTL/T/1282.

Julou L, Pasquet V and de M Mazuret, 1973 : Tolérance Locale chez le Lapin: PDMS 5000 cs. S.U.C.R.P. - D.S.Ph. N° 16710, 17062, 17064, 17400 and 17494, Rhône Poulenc, France.

Kellner TP, Hanes MA and Fruin JT, 1982. Primary occular irritation of two CHF1 formulations components: Dow Corning 200 and Isopropanol. Letterman Army Institute of Research. Technical Note No 82-31 TN.

Kennedy GL, Keplinger ML, Calandra JC and Hobbs EJ, 1976. Reproductive, teratologic and mutagenic studies with some polydimethylsiloxanes. J. Toxicol. and Env. Hlth 1 909-920 (These studies were carried out at Industrial Biotest Laboratory. They have been reviewed by Dow Corning and have been considered to be valid).

King WD and Siddiqui WH, 1989. A 90 day subchronic oral toxicity study with polydimethylsiloxane fluid in the mouse. DC Technical Report No 1989-I0003-2552. Dow Corning, Corp., Midland, Michigan, USA.

Kirk-Othmer, 1982. Encyclopedia of Chemical Technology, 3rd ed, 20, John Wiley & Sons, New York, USA.

Klein R, Annelin R and Varaprath S, 1994. Acute Toxicity of Emulsions of Dow Corning 50 cs PDMS Fluid with *Daphnia Magna*. DC Internal Report No 1994-I0000. Dow Corning Corp., Midland, Michigan, USA.

Klykken PA, Duwe RL, Galbraith TW and Isquith AJ, 1991a. Host resistance to Listeria Monocytogenes: Absence of an immuno-modulatory effect by 1000 cs Polydimethylsiloxane fluid. DC Technical Report No. 1991, I0000-36265. Dow Corning, Corp., Midland, Michigan, USA.

Klykken PA, Duwe RL, Galbraith TW and Isquith AJ , 1991b. Absence of an immunological reaction to Polydimethylsiloxane fluid. DC Technical Report No.1991-I0000-36322. Dow Corning, Corp., Midland, Michigan, USA.

Kreshkov AP, 1962. Practical Handbook of Analysis of Monomers and Polymers of Organosilicon Compounds, Kreshkov Ed., State Publishing House of Chemical Literature, Moscow.

Kumar P, Vijayaraghavan R, Prakash S and Sritastava RK, 1984. Indian J. Pharm. Sci. 47 (1), 104-107.

Lane TH and Annelin RB, 1983. A model for estimating environmental distribution. Health & Environmental Sciences. Research Department August 23, 1983. Report to Dow Corning Corp., Midland, Michigan, USA.

Lehmann RG , 1993. Extraction of Silicones from Soil. Environ. Toxicol. Chem. 12, 1851-1853.

Lehmann RG, Varapath S and Frye CL, 1994a. Degradation of silicone polymers in soil. Submitted for publication to Env. Chem. Toxicol.

Lehmann RG, Varapath S and Frye CL, 1994b. Fate of silicone degradation products (silanols) in soil. Submitted for publication to Env. Chem. Toxicol.

Levier RR, 1988. Permethylated siloxane insect toxicants. Silicon chemistry. COREY-GASPAR - Ellis Howood Publishers - Chap. 15, 153-160.

Lipowitz J and Ziemelis MJ, 1976. Flammability of polydimethysiloxanes. Flammability and fire hazard properties. J. Fire & Flammability 7, 504-529.

Löser E, 1981. Baysilon-Öl M100. Untersuchungen zur akuten oralen Toxizität an mönnlichen und weiblichen Wistar-Ratten. Internal Report. Bayer AG, Leverkusen, Germany.

Maggi P and Alzieu C, 1977. Etude de la nocivité d'huiles Polydiméthylsiloxane à l'égard d'organismes marins. Science et Pêche, Bull. Inst. Pêches marit. 269, mai, 1-3.

Mann H, Ollenschläger B und Reichenbach-Klinke HH, 1977. Untersuchungen zur Wirkung von Siliconölen auf Regenbogenforellen. Fisch Umwelt 3, 19-22.

Manston SE, Siddiqui WH and Zimmer MA, 1989. 90 day subchronic rat toxicity study with Polydimethylsiloxane fluids in male rats, DC Technical Report No 1989-I0005-2564. Dow Corning Corp., Midland, Michigan, USA.

Matsui S, Murakami T, Sasaki T, Hirose Y and Iguna Y,1975. Activated sludge degradability of organic substances in the waste water of the Kashima petroleum and petrochemical industrial complex in Japan. Prog. Water Technol. 7, 645-659.

McDonald DE, Lanier GE and Deichman WB, 1960. The Subacute oral Toxicity to the Rat of Certain Polydimethylsiloxanes. AMA Archives of Industrial Health 21, 514-518.

Monnot G, 1982 PDMS 10 cs: Essais de Toxicité Aigue par voies orales et percutanées chez le rat. IFREB Report N° 209214. Rhône Poulenc, France.

Nagase H, Ose Y and Sato T, 1988. Possible methylation of inorganic mercury by silicones in the environment. Sci. Tot. Environ. 73, 29-98.

Neely WB, Branson DR and Blau GE, 1974. Partition coefficient to measure bioconcentration potential of organic chemicals in fish. Environ. Sci. Technol., 8, 1113-1115.

Neely, W.B. and Mackay, D, 1982. An evaluative model for estimating environmental risk. In K.L. Dickson, A.W. Maki and J. Cairns, eds. "Modeling the fate of Chemicals in the Aquatic Environment" Ann Arbor Science, Ann Arbor, MI, 127-143.

Newman PJ, Bowden AV and Bruce AM, 1989. Production, treatment and handling of sewage sludge. In : Dirkswager ed, Sewage sludge treatment and use : New Developments, Technology Aspects and Environmental Effects. Elsevier 1989.

Nielson WR, Heinlein JP and Haigh WG, 1975. Acaridical and insectisidal activity of various silicone fluids. TSCA 8(c) Submission 87-8215084.

Nosanchuk JS, 1968. Injected dimethylpolysiloxane fluid : a study of antibody and histologic response. Plastic and Reconstructive Surgery 42 (6) 562-565.

Olson KJ, 1957. Comparison of PDMS/100 cs Fluid treated and untreated in so far as Eye contact Irritation is concerned. DC Technical Report No 1957-I0065-1057-2. Dow Corning Corp., Midland, Michigan, USA.

Olson KJ and Sadek SE, 1962. Toxicity by subcutaneous injection of Dow Corning 200 Fluids. DC Technical Report No. 1962-I0065-1063-05. Dow Corning Corp., Midland, Michigan, USA.

Opperhuizen A, Van Der Velde EW, Gobas FAPC, Liem DAK, Van Der Steen JMD and Hutzinger O, 1985. Relationship between bioconcentration in fish and steric factors of hydrophobic chemicals. Chemosphere 14(11/12), 1871-1896.

Opperhuizen A, Damen HWJ, Asyee GM, Van Der Steen JMD and, Autzinger O, 1987. Uptake and elimination by fish of Polydimethylsiloxanes (Silicones) after dietary and aqueous exposure. Toxicol. Environ. Chem. 13, 265-285.

Palazzolo RJ, 1964. Skin Irritation Study on Dow Corning 200 Fluid 350 cs. Lot AA 5472. Industrial Bio Test Laboratories Inc. DC Confidential Report No. 1964-I0065-1059-01. Dow Corning Corp., Midland, Michigan, USA.

PARCOM Decision, 1992. On the Phasing out of PCBs and Hazardous PCB substitutes". Ministerial Meeting of the Oslo and Paris Commissions. Paris, 21-22 September 1992.

Parker RD and Tapschott DJ, 1993. Water solubilities of DC 200/350 cSt and DC 200/1000 CST fluids. DC International report 1993-10000 38330, 19 August 1993. Dow Corning Corp., Midland, Michigan, USA.

Pauluhn J, 1985. Silikonoel AK 100,000. Untersuchungen zur akuten Inhalationstoxizität. Report No. 13213. Bayer AG, Wuppertal, Germany.

Pauluhn J, 1990, Baysilone M 10000. Untersuchungen zur akuten Inhalationstoxizität an der Ratte nach OECD Richtlinie No. 403. Report No. 18934. Bayer AG, Wuppertal, Germany.

Pellenbarg RE, 1979a. Silicones as traces for anthropogenic additions to sediments. Marine Poll. Bull. 10, 267-269.

Pellenbarg RE, 1979b Environmental Poly(organosiloxanes) (silicones). Env. Sci. Technol. 13, 565-569.

Pellenbarg RE, 1982. Silicones in Chesapeake Bay sediments. Mar. Poll. Bull. 13, 427-429.

Pellenbarg RE and Cahart HW, 1990. Bioturbation recorded by a sedimentary siloxane horizon. Appl. Organomet. Chem. 4, 177-180.

Pellenbarg RE and Tevault DE, 1986. Evidence of sedimentary siloxane horizon. Env. Sci. Tecnol. 20,743-744.

Pellanbarg RE and Tevault DE, 1988. Silicone as a trace contaminant in laboratory solvents. Sci. Tox. Environ. 73, 23-27.

Plotzke KP and Mc Mahon JM, 1994. Feasability study: *In vivo* percutaneous absorption of ^{14}C-polydimethyl siloxane fluid, 350 cs in the male rat. DC Technical Report No 1994-I0000/38932. Dow Corning Corp., Midland, Michigan, USA.

Rast HG, 1993. Private communication. ZF-Chemische Forschung. Bayer AG, Leverkusen/Germany.

Reed WA and Kittle CF, 1959. Observations on Toxicity and Use of Antifoam A. Arch. of Surgery 78, 220-225.

Refojo MF, Rolden M, Leong F-L and Henriquez AS, 1985. Effect of silicone oil on the cornea. J. Biomed. Mater. Res. 19, 643-652.

Reuse J, 1979. PDMS and glucose absorption. DC Technical Report No. 1979-I9039-14. Dow Corning Corp., Midland, Michigan, USA.

Rondot G, 1985a. PDMS 20 cs: Essais de Toxicité Aigue par voies orales chez le rat. Hazleton IFT Report N° 507266. Rhône Poulenc, France.

Rondot G, 1985b. PDMS 50 cs: Essais de Toxicité Aigue par voies percutanées chez le rat. Hazleton IFT Report N° 501251. Rhône Poulenc, France.

Rondot G, 1985c. PDMS 500 cs: Essais de Toxicité Aigue par voies percutanées chez le rat. Hazleton IFT Report N° 501247. Rhône Poulenc, France.

Rondot G, 1985d. PDMS 1000 cs: Essais de Toxicité Aigue par voies percutanées chez le rat. Hazleton IFT Report N° 501246. Rhône Poulenc, France.

Rowe V, Spencer HC and Bass SL, 1948. Toxicological Studies on Certain Commercial Silicones and Hydrolyzable Silane Intermediates. J. Ind. Hyg. and Toxicol. 30, 332-352.

Rowe V, Spencer HC and Bass SL, 1950. Toxicologic Studies on Certain Commercial Silicones II. Two year dietary feeding of "DC Antifoam A" to rats. Arch. Ind. Hyg. and Occup. Med. 1 539-544.

Ryan JW, 1988. Analysis of Fluids from Septic Tanks. DC Technical Report No. 1988-I0030-6305. Dow Corning Corp., Midland, Michigan, USA.

Schoenig G, Fancher OE and Calandra JC, 1967. Range Finding Eye Irritation Test on Dow Corning 200 Fluid, 10 cs. DC Technical Report No 1967-I0065-1056-3. Dow Corning Corp., Midland, Michigan, USA.

Sharp, RF and Eggins, HOW, 1970. A biodeterioration appraisal of silicones. Int. Biodegrad. Bull. 6 (1), 19-26.

Siddiqui WH, Annelin RB, Stanton E, Kolesar GB and Devries CR, 1984. DC Report 1984, I0005-1230. Dow Corning Corp., Midland, Michigan, USA.

Siebert F, 1988. Verteilung von Siliconen in der Umwelt (Sedimente, Böden aund Klärschlämme inter Bundesrepublik Deutschland). Thesis, University of Heidelberg.

SIA, 1982. Organo Silicone Compounds in the environment. Silicone Industry Association of Japan.

Smith AL, 1980. Correspondence. Wat. Pollut. Control. 79, 146-147.

Smith AL, 1991. The Analytical Chemistry of Silicones. John Wiley & Sons, Inc, New York.

Sommerlade R, Parlar H, Wrobel D and Kochs P, 1993. Product Analysis and Kinetics of the Gas-Phase Reactions of Selected Organosilicon Compounds with OH Radicals Using a Smog Chamber-Mass Spectrometer System. Environ. Sci. Technol. 27, 2435-2440.

Spacie A, 1972. Acute toxicity of SAG 10 and SAG 350 silicone antifoam to aquatic organisms. Internal Report, Union Carbide Chemicals Corp., Danbury, USA.

Springborn, 1991. Octamethylcyclotetrasiloxane - the subchronic toxicity to midge larvae under flow-through conditions. Report of Springborn Lab. to Silicone Health Council, SLI Report 91-3-3698, Wareham/MA, USA 10. April 1991.

Stanton E, 1983. Intraperitoneal administration of PDMS Fluids in rabbits. DC Technical Report No 1983-I0065-2061-06. Dow Corning Corp., Midland, Michigan, USA.

Stanton E, 1984. Acute toxicological properties and Industrial handling hazards of Dow Corning 200 Fluid, 50 cs. DC Confidential Report No. 1984-I0005-1193. Dow Corning Corp., Midland, Michigan, USA.

Street JR, 1980. Assessment of the biochemical oxygen demand of Dow Corning polydimethylsiloxane fluid. ICI Brixham Laboratory, DC Report n° BL/B/2078. Dow Corning Corp., Midland, Michigan, USA.

Suberg H, 1984a. Baysilicone M1000. Prüfung auf primär reizende/ätzende Wirkung and der Kaninchenhaut. Cited in Bayer Report. Bayer AG, Germany.

Suberg H, 1984b. Baysilicone M1000. Prüfung auf primär reizende/ätzende Wirkung anm Kaninchenauge. Internal Report. Bayer AG, Leverkusen, Germany.

Suskind, RR, 1954. Industrial and laboratory of a silicone protective cream. Arch. Ind. Hyg. & Occup. Med.101.

Thyssen J, 1980. Untersuchungen zur Haut- und Schleimhautverträglichkeit. Internal Report.
Bayer AG, Leverkusen, Germany.

Tsuchitani Y, Harada K, Sato K, Muramatsu N and Uematsu K, 1978. Determination of organosilicone in sewage sludge by atomic absorption spectrometry. Bunseki Kagaku 27, 343-347.

Ullman, 1993. Silicones. Encyklopädie der technischen Chemie. Verlag Chemie, Weiheim, Germany, A24, 57-93.

Union Carbide, 1953. Range Finding Tests on dimethylsilicone oil L-45. Carnegie-Mellon Inst. of Res., Univ. of Pittsburgh. Report No. 16-64. Union Carbide Chemicals Corp., Danbury, USA.

Union Carbide, 1978. Toxicity and Irritation Assay results of some Food, Drug or Cosmetic Product Chemicals. Silicone L-45 Fluid. Carnegie-Mellon Inst. of Res, Univ. of Pittsburgh. Report No. 41-138. Union Carbide Chemicals Corp., Danbury, USA.

US-EPA, 1992. NTP Report on the Immunotoxicity of polydimethylsiloxane in Female B6C3F1 Mice (Contact Hypersensitivity Studies) cited in 13th Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency.

Van der Post DC, 1978. Aspects of Silicone Oil as a Water Pollutant. Wat. Pollut. Control. 520-524.

Van der Post DC, 1979. Some Effects of Silicone Oil Pollution on the Aquatic Environment. Wat. Pollut. Control, 389-394.

Varaprath S, Frye CL and Hamelink JL, 1994. Aqueous solubility of the oligomeric permethyl siloxanes. Submitted for publication to Environ. Sci. Technol.

Veith GD, Defoe, DL and Bergstedt BV, 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. J.Res.Board Can. 36, 1040-1048.

Wacker, 1992. Wacker-Broschüre: Silicone Fluids AK, Wacker Chemie AG, München, Germany.

Wacker, 1994. Safety Data Sheet: Wacker Silicone Fluid AK 350. Wacker Chemie AG, München, Germany.

Wasserbauer R and Zadak Z, 1990. Growth of *Pseudomonas putida* and *P. fluorescens* on silicone oils. Folia Microbiol. 35, 384-393.

Watanabe N, Nakamura T, Watanabe E, Sato E and Ose Y, 1984a. Bioconcentration potential of Polydimethylsiloxane (PDMS) fluids by fish. Sci. Total Environ. 38, 167-172.

Watanabe N, Nakamura T, Watanabe E, Sato E and Ose Y, 1984b. Distribution of organosiloxanes (silicones) in water, sediments and fish from the Nagara River Watershed, Japan. Sci. Total Environ. 35, 91-97.

Watanabe N, Yasuda Y, Kato K, Nakamura T, Funasaka R, Shimokawa K, Sato E and Ose Y, 1984c. Determination of trace amounts of siloxanes in water, sediments and fish tissues by inductively coupled plasma emission spectroscopy. Sci. Tot. Environ. 34, 169-176.

Watanabe N, Sato E and, Ose Y, 1985a. Adsorption and desorption of polydimethylsiloxane, PCBS, cadmium nitrate, copper sulfate, nickel sulfate and zinc sulfate by river surface sediments. Sci. Tot. Environ. 41, 153-161.

Watanabe N, Nagase H, Ose Y, Sato E, 1985b. Identification of silicones in field samples, anti-foaming agent, car polish, and cosmetics by gel filtration - inductively coupled plasma emission spectrometry (ICP). Esei Kagaku 31, 391-396.

Watanabe N, Nagase H, Nakamura T, Watanabe E and Ose Y, 1986. Chemical methylation of Mercury (II) salts by polydimethylsiloxanes in aqueous solution. Ecotox. Environ. Safety 11, 174-178.

Watts RJ, Haling CS and Gearhart L, 1993. Fate and effects of Polydimethysiloxanes on wastewater treatment processes. Report from Washington State University Pullmann/WA to Dow Corning Corp., Midland, Michigan, USA.

Weschler CJ, 1981. Identification of selected organics in the arctic aerosols. Atmosph. Environ. 15, 1365-1369.

Weschler CJ, 1988. Polydimethylsiloxanes associated with indoor and outdoor airborne particles. Sci. Tox. Environ. 73, 53-56.

Wollast, 1979. Laboratory of Environmental Sciences, Brussels University. DC Internal Report I9039-1-1979.

Zitko V and Hutzinger O, 1976. Uptake of chloro- and bromobiphenyls, hexachloro and hexabromobenzene by fish. Bull. Environ. Contam. Toxicol. 16(6), 665-673.

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No. 13	Joint Assessment of Commodity Chemicals, (HFA-123) 1,1-Dichloro-2,2,2-Trifluoroethane. May 90
No. 14	Joint Assessment of Commodity Chemicals, (HFA-133a) 1-Chloro-2,2,2-Trifluoromethane. Aug 90
No. 15	Joint Assessment of Commodity Chemicals, (HFA-141B) 1-Fluoro 1,1-Dichloroethane. Aug 90
No. 16	Joint Assessment of Commodity Chemicals, (HCFC-21) Dichlorofluoromethane. Aug 90
No. 17	Joint Assessment of Commodity Chemicals, (HFA-142b) 1-Chloro-1,1,Difluoroethane. Feb 91
No. 18	Joint Assessment of Commodity Chemicals, Vinylacetate. Feb 91
No. 19	Joint Assessment of Commodity Chemicals, Dicyclopentadiene. Jul 91
No. 20	Joint Assessment of Commodity Chemicals, Tris-/Bis-/Mono-(2-ethylhexyl)phosphate. May 92
No. 21	Joint Assessment of Commodity Chemicals, Tris-(2-butoxyethyl)-phosphate. Mar 92
No. 22	Joint Assessment of Commodity Chemicals, Hydrogen Peroxide. Jan 93
No. 23	Joint Assessment of Commodity Chemicals, Polycarboxylate Polymers as Used in Detergents. Nov 93
No. 24	Joint Assessment of Commodity Chemicals, (HFC-125) Pentafluoroethane. May 94
No. 25	Joint Assessment of Commodity Chemicals, (HCFC-124) 1-Chloro-1,2,2,2-Tetrafluoroethane. Jul 94
No. 26	Joint Assessment of Commodity Chemicals, Linear Polydimethylsiloxanes (viscosity 10-100,000 centisokes). Sep 94
No. 27	Joint Assessment of Commodity Chemicals, *n*-Butyl Acrylate. CAS No. 141-32-2. Aug 94

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