**Factsheets on**

**alternatives to perfluorooctane sulfonic acid,**

**its salts and perfluorooctane sulfonyl fluoride**

**Second draft**

**(6 June 2014)**

**Note:**

This document contains a compilation of draft factsheets developed as part of the assessment of alternatives to perfluorooctane sulfonic acid,(PFOS), its salts and perfluorooctane sulfonyl fluoride (PFOSF). The fact sheets provide an analysis on a screening level as to whether or not the identified alternatives to PFOS meets the numerical thresholds in Annex D, but does not analyze monitoring data or other evidence as provided for in Annex D. So failure to meet the thresholds should be considered as a likelihood rather than as evidence that the alternative to PFOS is not a Persistent Organic Pollutant (POP). Explanations about the methodology for developing the factsheets are contained in the draft report on the assessment of alternatives to PFOS, its salts and PFOSF. The conclusions section of the factsheets summarises the evidence base for the conclusions regarding whether Annex D criteria are met. More detailed description of the supporting evidence with references are provided in the summary of data section of the factsheets.

**Contents**

1. Decamethyl cyclopentasiloxane (D5) 3

2. Decamethyl tetrasiloxane (MD2M) 11

3. Diisopropyl-1,1'-biphenyl 17

4. Diisoproplynaftalene (DIPN) 22

5. Dodecamethyl cyclohexasiloxane (D6) 28

6. 1-Isopropyl-2-phenyl-benzene 35

7. Octamethyl cyclotetrasiloxane (D4) 40

8. Octamethyl trisiloxane (MDM) 48

9. Triisopropylnaftalene (TIPN) 55

# Decamethyl cyclopentasiloxane (D5)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

## Persistence

A biodegradation study indicates a degradation rate of 0.14% in 28 days in water. This result indicates that D5 slowly degrades in water likely with a persistence half-life more than 2 months.

Sediment degradation half-lives of 1200 days under aerobic conditions at 24°C and 3100 days under anaerobic conditions at 24°C were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with Good Laboratory Practices (GLP).

D5 is therefore considered to fulfil the persistence criteria according to Annex D 1 (b) (i).

## Bioaccumulation

A steady-state bioconcentration factor (BCF) value of 7060 for fathead minnows was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP.

D5 is therefore considered to fulfil the bioaccumulation criteria according to Annex D 1 (c) (i).

## Long-range transport (LRT)

D5 has the potential to be transported over long-distances in the atmosphere. In air, D5 is persistent with calculated atmospheric half-lives of more than 3 days.

Therefore D5 is considered to fulfil the Annex D 1 (d) (iii) criteria.

## Ecotoxicity

D5 shows essentially no acute toxicity to aquatic organisms with no observed effect concentration (NOEC) of ≥14 µg/L (Oncorhynchus mykiss) and a NOEC of ≥2.9 ( *Daphnia magna*) when tested at concentrations up to its water solubility limit. A 28 day effect concentration for terrestrial organisms lethal concentration (LC50) and NOEC > 4000 mg/kg dry weight indicate no terrestrial toxicity.

D5 is therefore not likely to fulfil the Annex D 1 (e) (ii) criteria.

## Toxicity to human health

D5 has not been classified by the [International Agency for Research on Cancer](http://www.google.se/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=8&cad=rja&uact=8&ved=0CEgQFjAH&url=http%3A%2F%2Fen.wikipedia.org%2Fwiki%2FInternational_Agency_for_Research_on_Cancer&ei=N52JU_XKGun14QSwt4BI&usg=AFQjCNEYL6xdRwVGiQLGW21eKY-D5d7WMQ&sig2=SdQLe4twYeXyLEwJMkfmVQ&bvm=bv.67720277,d.bGE) (IARC) for carcinogenicity. No international agency has classified D5 for reproductive/developmental toxicity. Data on the endpoints for carcinogenity, genotoxicity and reproductive/developmental toxicity show no toxicity.

D5 is therefore not likely to fulfil the Annex D 1 (e) (ii) criteria.

**SUMMARY OF DATA**

## Identity of the substance and physical and chemical properties

1. **Name and other identifiers of the substance**

Table 1: Substance identity [2]

|  |  |
| --- | --- |
| Common name: | Decamethyl cyclopentasiloxane (D5) |
| IUPAC name: | 2,2,4,4,6,6,8,8,10,10-decamethyl-1,3,5,7,9,2,4,6,8,10-pentaoxapentasilecane |
| CAS number: | 541-02-6 |
| Molecular weight: | 370.8 g/mol |
| Chemical structure: | ChemSpider 2D Image | Decamethylcylopentasiloxane | C10H30O5Si5 |

1. **Chemical group**

Cyclic volatile methyl-siloxanes (cVMS)

1. **Physico-chemical properties**

Table 2: Overview of selected physico-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure  | Experimental:26.66(0.20 mm Hg)Experimental:33.2\*(0.249 mm Hg)Modelled: 29.06(0.22 mm Hg) | [1] |
| Water solubility | <5 μg/L at 25°C. | [4] |
| Partition coefficient n-octanol/water (log value) | Experimental: 4.76 at 22.4°C5.2 8.03 at 25.3°CModelled: 5.71 | [1] |
| Partition coefficient air/water Partition coefficient (log value) | Experimental: 3.13 at 24.6°C |  [1] |
| Partition coefficient air/octanol (log value) | 5.06 at 24°C  | [1] |
| Henry’s Law Constant | Experimental3 350 000\*(33.1 atm·m3/mol)13 444(0.133 atm·m3/mol)  at 23°C32 317(0.319 atm·m3/mol)at 26°CExperimental:29 831(0.294 atm·m3/mol) at 26°CModelled: 12 159(0.12 atm·m3/mol) at 25°C | [1] |

## Classification and labelling

1. Classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) [5]

Regulation (EC) No 1272/2008

No harmonized classification available.

## Environmental fate properties

A biodegradation rate of 0.14% in 28 days in water, i.e. no biodegradation observed under test conditions, was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [11].

Sediment degradation half-lives of 1200 days under aerobic conditions at 24°C and 3100 days under anaerobic conditions at 24°C were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. The major degradation products, under aerobic and anaerobic conditions, were dimethylsilanediol and non-extractable silanols, while carbon dioxide and methane generation was minimal, indicating complete mineralisation of D5 or its degradation products is very slow [11].

Under aerobic conditions in sediment, D5 degradation in non-sterilised samples was significantly faster than that in the chemically sterilised samples, suggesting that the degradation of D5 in the sediment might not be purely abiotic [11].

Half-life on Wahiawa soil of 0.08 days was determined in a reliable study conducted according to an appropriate test protocol [11].

D5 was found to hydrolyse rapidly in air-dried soil to form degradation intermediates in a reliable study conducted according to generally accepted scientific principles. Given sufficient time, these degradation intermediates ultimately hydrolysed to dimethylsilanediol [11].

Half-lives in temperate soil of 9.7 to 12.5 days (depending on relative humidity) and in tropical soil of 0.11 to 0.19 days (depending on relative humidity) were obtained using accepted calculation methods. The results are considered to be reliable [11].

## Phototransformation/photolysis

No data available.

## Biodegradation

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water  | < 0.14% in 28 days> 182 | [11]Epi Suite, level III fugacity model |
| Soil  | <182 | Epi Suite, level III fugacity model |
| Sediment | 1200365 | [11]Epi Suite, level III fugacity model |

## Potential for long range transport

D5 has the potential to be transported over long-distances in the atmosphere. In air, D5 is persistent with calculated atmospheric half-lives of more than 3 days [1].

## Bioaccumulation

A steady-state BCF value of 7060 and kinetic BCF value of 13000 for fathead minnows were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [11].

## Human health hazard assessment

|  |  |
| --- | --- |
| **Health hazard** | **References**  |
| 1. Acute toxicity
 |  |
| An acute oral lethal dose, LD50 value of >5000 mg/kg for male and female rats was determined in a reliable study conducted according to an appropriate test protocol.An acute inhalation LC50 value of 8.67 mg/L was determined for male and female rats in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. In a study that was conducted according to the Organization for Economic Co-operation and Development (OECD), 403 but was not compliant with GLP, the acute inhalation LC50 value for rats was greater than the highest achievable vapour concentration, corresponding to 545 ppm (ca. 6.72 mg/L). An acute dermal LD50 value of >2000mg/kg was determined for male and female rabbits in a reliable study conducted according to an appropriate test protocol. Not conducted according to GLP.An acute inhalation LC50 value of 8.67 mg/L was determined for male and female rats in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. | [11][11][11] |
|  |  |
| 1. Mutagenicity
 |  |
| The test article, under the experimental conditionsreported, did not demonstrate genetic activity, both with and without metabolic activation. Decamethylcyclopentasiloxane is therefore considered to be non-mutagenic in the Salmonella typhimurium and Escherichia coli reverse mutation assay.In a highly reliable test, conducted in accordance with OECD 473 under GLP conditions, the test article did not induce structural chromosome aberrations in V79 cells (Chinese hamster cell line) in vitro. Decamethylcyclopentasiloxane is therefore considered to be non-clastogenic when tested up to cytotoxic concentrations in the absence of metabolic activation and up to the highest recommended concentrations in the presence of metabolic activation.One *in vivo* test reported in conclusion under the experimental conditions that the test article did not increase levels of micronucleated rat bone marrow cells of the treated rats. Therefore, the test article is considered to benon-genotoxic in this study. | [8][11] |
|  |  |
| 1. Carcinogenity
 |  |
| There is no IARC classification on cancer for D5.  | [6] |
| In a two-year inhalation combined chronic toxicity and carcinogenicity study in rats conducted to an EPA guideline and to GLP (reliability score 1) the [No Observed Adverse Effect Concentration](http://www.google.se/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=1&ved=0CC8QFjAA&url=http%3A%2F%2Fwww.acronymfinder.com%2FNo-Observed-Adverse-Effect-Concentration-(NOAEC).html&ei=_5-JU9H4KqaD4gSS8ICABw&usg=AFQjCNEpTzvPZWMxH8cp1l-UR8rXNbHvZA&sig2=U7H2Ir3pDUAz0WGxUL_kXw&bvm=bv.67720277,d.bGE) (NOAEC) for general toxicity was ≥160 ppm (2.42 mg/L; the highest dose tested). Local effects on the nasal cavity and adaptive increases in liver weights (with no microscopic findings) in females were observed at 160 ppm. The NOAEC for carcinogenic effects was 40 ppm (0.6 mg/L) based on uterine tumours (endometrial adenocarcinoma) at 160 ppm. | [1][11] |
| In a chronic toxicity and carcinogenicity study, rats were exposed to vapour concentrationsof 0, 10, 40 or 160 ppm D5 for 6 h/day, 5 days/week for 24 months. In the highest dosegroup, there was a statistically significant increase in uterine tumours (endometrialadenocarcinomas) observed in female rats in the highest exposure group and an increasedincidence of hyaline inclusions in the nasal respiratory/olfactory epithelium of both sexes. | [1] |
|  |  |
| Also, a subgroup exposed to the same concentrations for 12 months with a 12-monthrecovery period showed an increased incidence of hyaline inclusions in the nasalrespiratory/olfactory epithelium of both sexes at 40 and 160 ppm.Decamethylcyclopentasiloxane (D5) was not genotoxic in several *in vitro* and *in vivo* assays The limited genotoxicity results suggest that the tumours observed, could be due to threshold effects. | [1] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| No international agency has classified D5 for reproductive/developmental toxicity. In a two-generation reproductive toxicity study (reliability score 1) conducted to appropriate EPA test guidelines and to GLP, no parental toxicity in the F0 and F1 generations was observed at exposure concentrations of 30, 70, and 160 ppm. F0 and F1 reproductive performance was not affected at any concentration. No test-substance-related total litter losses occurred, and no neonatal toxicity was evident in the F0 and F1 generations at concentrations of 30, 70, and 160 ppm.  | [3][11] |
|  |  |
| 1. Neurotoxicity
 |  |
| No F2 developmental neurotoxicity was evident at any concentration. Based on the results of this study, the NOAEL for parental toxicity, reproductive toxicity, neonatal toxicity, and developmental neurotoxicity is considered to be at least 160 ppm. | [11] |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available  |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available  |  |
|  |  |
| Mode of action |  |
| It is recognized that D5 may possibly act as a dopamine agonist, thus contributing to the observed tumourigenic effects in female rats. | [1] |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| The critical effect level for repeated-dose toxicity is considered to be 100 mg/kg-bw/day via the oral route. This is based on increased liver weights in a 90-day rat study, as well as the extrapolation of critical effects and levels from oral data on the similar compounds D4 and D6 to D5.  | [3] |

## Environmental hazard assessment

Aquatic compartment (including sediment)

D5 shows essentially no acute toxicity to aquatic organisms when tested at concentrations

up to its water solubility limit [1].

A 96-h LC50 value of >16 µg a.i./L has been determined for the effects of the test substance on mortality of Oncorhynchus mykiss under flow-through exposure conditions. A NOEC of ≥16 µg a.i./L has been determined in the same test. Continuation of exposure to a total of 14 days resulted in the same values [11].

A 90-day (60-day post-hatch) NOEC of ≥14 μg/L has been determined for the effects of the test substance on hatching and larval survival and growth of Oncorhynchus mykiss under flow-through exposure conditions [11].

A 48-hour EC50 value of >2.9 µg a.i./L has been determined for the effects of the test substance on mobility of Daphnia magna. A NOEC of ≥2.9 µg a.i./L has been determined in the same test [11].

A 21-day NOEC of ≥15µg/L has been determined for the effects of the test substance on survival, reproduction and growth of Daphnia magna [11].

An ASRI 3hr EC50 of >2000 mg/L was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [11].

A 28-Day LC50 value of 257 mg/kg dry weight has been determined for the effects of the sediment incorporated test substance on mortality of Chironomus riparius. A NOEC of 70 mg/kg dry weight for effects on development rate and a NOEC of 160 mg/kg dry weight for effects on development time and emergence ratio have been determined in the same test [11].

Terrestrial compartment

A 28-day LC50 value of >4074 mg/kg dry weight and a 56-day NOEC of ≥4074 mg/kg dry weight have been determined for the effects of the test substance on mortality and reproduction and growth respectively of *Eisenia andrei* [11].

## Other information

A search in Scopus yielded 15 peer reviewed articles with focus on health and environment for D5 [8].

Following a Board of Review process, Environment Canada concluded that decamethylcyclopentasiloxane (D5) does not meet the legal definition of toxic. Based on the available scientific data, D5 was considered persistent in air, water and sediments but not in soils. Additionally, while new data have increased the confidence that D5 has the potential to accumulate in organisms, this behaviour does not appear to cause ecological harm at environmentally relevant concentrations [13].

The ECHA PBT Expert Group concluded that D5 meets the Annex XIII criteria in the EC Regulation No 1907/2006 (REACH), for a ‘very persistent and very bioaccumulative (vPvB) substance in the environment due to its persistence in sediment and a high bioconcentration factor in fish. Although the T criteria are not met, there are some uncertainties relating to the limited available data on mammalian, avian and fish reproductive effects, and toxicity has been observed in sediment and soil organisms [12].

## References

[1] Environment Canada Health Canada, Screening Assessment for the Challenge

Decamethylcyclopentasiloxane (D5), (2008)

<http://www.ec.gc.ca/ese-ees/13CC261E-5FB0-4D33-8000-EA6C6440758A/batch2_541-02-6_en.pdf>

[2] Chemspider, <http://www.chemspider.com/Chemical-Structure.10451.html>

[3] European Commission, Scientific Committee on Consumer Safety (SCCS) , “OPINION ON Cyclomethicone Octamethylcyclotetrasiloxane Cyclotetrasiloxane, D4) and Decamethylcyclopentasiloxane (Cyclopentasiloxane, D5)”, (2010)

[4] Environmental Agency UK, ”Environmental Risk Assessment Report: Decamethylcyclopentasiloxane” ISBN: 978-1-84911-029-7, (2009)

[5] Harmonized Classification according to GHS Regulation (EC) No 1272/2008

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[6] International Agency for Research on Cancer (IARC)

<http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[7] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[8] Scopus, primary literature screening search, <http://www.scopus.com/home.url?zone=header&origin=resultslist>

[9] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[10] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[11] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

 [12] The EU PBT Working Group assessment report on decamethyl cyclopentasiloxane (D5) (2012)

<http://echa.europa.eu/documents/10162/13628/octamethyl_pbtsheet_en.pdf>

[13]Siloxane D5 (Cyclopentasiloxane, decamethyl-) notice February 2012. <http://gazette.gc.ca/rp-pr/p1/2012/2012-02-25/html/notice-avis-eng.html#d121>

# Decamethyl tetrasiloxane (MD2M)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

## Persistence

One experimental data point indicates high persistence in water for decamethyl tetrasiloxane, with a biodegradation rate of 0% in 28 days in water. The substance likely degrades rather fast in soil depending on the water content (1.48 days at 32%RH and 119.5 days at 100%RH) [9]. There is no data available for degradation in sediment.

Decamethyl tetrasiloxane (MD2M)cannot therefore be assessed towards the Annex D 1 (b) (i) criteria due to equivocal data.

1. **Bioaccumulation**

Steady-state experimental BCF values of 3870 L/kg (0.43 µg/L) and 1610 L/kg (5.3 µg/L) in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP.

Decamethyl tetrasiloxane (MD2M) is considered not to fulfil the bioaccumulation criteria according to Annex D 1 (c) (i).

1. **Long-range transport (LRT)**

Estimated half-life in air is 7.150 Days [AopWin v1.92].

Decamethyl tetrasiloxane (MD2M) is considered to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

 The LC50 and NOEC values available indicate that MD2M is not toxic to aquatic organisms and terrestrial organisms up to the solubility limit of the substance.

Decamethyl tetrasiloxane (MD2M) is not likely to fulfil the Annex D 1 (e) criteria.

1. **Toxicity to human health**

MD2M has an LOD > 2000 mg/kg which indicate low acute toxicity. MD2M has not been classified by IARC for carcinogenicity. Data on the endpoints for carcinogenity, genotoxicity and reproductive/developmental toxicity show no toxicity effect.

Decamethyl tetrasiloxane (MD2M) is not likely to fulfil the Annex D 1 (e) criteria.

**SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [3]

|  |  |
| --- | --- |
| Common name: | Decamethyl tetrasiloxane (MD2M) |
| IUPAC name: | Decamethyltetrasiloxane |
| CAS number: | 141-62-8 |
| Molecular weight: | 310.69 g/mol |
| Chemical structure: | http://images-a.chemnet.com/suppliers/chembase/189/189180_1.gif |

1. **Chemical group**

Linear volatile methyl siloxanes (linear VMS)

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Experimental: 52 Pa (20° C)73 Pa (25° C)Estimated:64.8 Pa (25°C) | [9]Epi Suite v 1.43 |
| Water solubility | Experimental: 0,00674 mg/LEstimated: 0.002918 mg/L |  [9]Epi Suite v 1.42 |
| Partition coefficient n-octanol/water (log value) | Exper.8.21Estimated: 8.21 |  [9]Epi Suite v 1.68 |
| Partition coefficient air/water (log value) | Estimated:2.842 | Epi Suite v 1.10 |
| Partition coefficient air/octanol (log value) | Estimated: 5.368 | Epi Suite v 1.10 |
| Henry’s Law Constant | No data available  |  |

1. **Classification and labelling**
2. Harmonized Classification according to GHS

Regulation (EC) No 1272/2008 [2]

No harmonized classification available

1. **Environmental fate properties**

A biodegradation rate of 0% in 28 days in water was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [9].

Soil degradation rates were determined for two different soil types in a reliable study conducted according to generally accepted scientific principles. In air-dried Michigan Londo soil, half-lives (closed tubes) ranged from 1.48 days at 32% RH to 119.5 days at 100% RH at 22.5°C. In air-dried UK loamy silt soil, half-life (closed tubes) was 0.26 days at 32% RH. In open systems, up to one third of the substance was lost by volatilisation, the amount lost increasing with RH. In open systems volatilisation at 32% RH was not significant, and degradation was rapid at this RH in both open and closed systems, but at 100% RH volatilisation was the predominant removal process (half-life <1days) [9].

1. **Phototransformation/photolysis**

No data available.

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | 38 | Epi Suite, level III fugacity model |
| Soil  | 0.26 (32% RH)< 1 (100% RH)75 | [9]Epi Suite, level III fugacity model |
| Sediment | 338 | Epi Suite, level III fugacity model |

1. **Potential for long range transport**

Estimated half-life in air is 7.150 days [AopWin v1.92] [3] which indicates that MD2M may have the potential for long range transport.

1. **Bioaccumulation**

Steady-state BCF values of 3870 L/kg (0.43 µg/L) and 1610 L/kg (5.3 µg/L) and kinetic BCF values of 3830 L/kg (0.43 µg/L) and 1760 L/kg (5.3 µg/L) were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [9].

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References** |
| 1. Acute toxicity
 |  |
| An LD50 value of >2000 mg/kg (oral) was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. | [9] |
| An acute dermal LD50 value of >2000 mg/kg was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. | [9] |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| Decamethyltetrasiloxane has been tested according to OECD TG 476 and under GLP conditions for mutagenicity to mouse lymphoma L5178Y cells up to cytotoxic concentrations. No increase in mutant frequency was detected at any concentration after 4h exposure with and without metabolic activation and 24 h exposure without metabolic activation. Appropriate solvent and positive controls were included and gave expected results. It is concluded that the test substance is negative for the induction of mutations in L5178Y cells under the conditions of the test. | [9] |
| No cancer classification according to IARC available | [4] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| In a combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test conducted using a protocol comparable to OECD 422 and to GLP (reliability score 1) the NOAEC for general and reproductive toxicity was at least 400 ppm (the only concentration tested) according to the study report. However, it should be noted that three female rats in the 400 ppm group with evidence of copulation failed to deliver a litter. One of these three females showed signs of parturition (blood discharge) on gestation day 25, but no pups were found. However, seven implant sites were present. The remaining females produced litters that were similar to the controls. | [9] |
| In a combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test conducted using a protocol comparable to OECD 422 and to GLP (reliability score 1) the NOAEC for general and developmental toxicity was at least 400 ppm (the only concentration tested) according to the study report. | [9] |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available |  |
|  |  |
| 1. Mode of action
 |  |
| No data available |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| No data available |  |
|  |  |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

A 96-hour LC50 value of >6.3 μg/L and NOEC of ≥6.3 μg/L have been determined for the effects of the substance on mortality of Oncorhynchus mykiss based on mean measured concentrations [9].

A 35-day LC50 value of >6.7 μg/L (nominal), >5.3 μg/L (mean measured) and NOEC of ≥6.7 μg/L (nominal), ≥5.3 μg/L (mean measured) have been determined for the effects of the test substance on mortality of Pimephales promelas [9]. A 21-day EC50 of >4.9 μg/L and NOEC of ≥4.9 μg/L have been determined for the effects of the test substance on adult mortality, reproduction and growth of Daphnia magna, based on measured values [9].

An EC50 value of >100 mg/L for toxicity to microorganisms was determined in a reliable ASRI study conducted according to an appropriate test protocol, and in compliance with GLP [9].

No effects on growth and survival have been reported when testing the registered substance at a loading rate of 100 mg/kg dwt sediment (68 mg/kg dwt mean measured) with the freshwater amphipod *Hyallela azteca*. Therefore 28-day NOEC and LC50 values of ≥68 and >68 mg/kg have been determined respectively in a sediment containing 3.7% organic carbon [9].

Terrestrial compartment

A 28-day LC50 value of 813 mg/kg dry weight and a 28 day IC50 value of 767 mg/kg dry weight have been determined for the effects of the test substance on mortality and reproduction of *Folsomia candida*. A NOEC of 377 mg/kg dry weight has been determined by the reviewer on the basis of a visual examination of the data for both mortality and reproduction [9].

1. **Other information**

A search in Scopus yielded 5 peer reviewed articles with focus on health and environment for MD2M [7]. The primary record for MD2M was not found in the TOXNET HSDB database [8].

1. **References**

[1] Chemnet, global chemical network, <http://www.chemnet.com/cas/supplier.cgi?terms=Decamethyl+tetrasiloxane+&l=en&exact=dict&f=plist&mark=&submit.x=24&submit.y=18>

[2] Harmonized Classification according to GHS Regulation (EC) No 1272/2008,

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[3] Chemspider, <http://www.chemspider.com/>

[4] International Agency for Research on Cancer (IARC), <http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[5] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[6] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[7] Scopus, primary literature screening search, http://www.scopus.com/home.url?zone=header&origin=resultslist

[8] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[9] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

[10] Nite, Incorporated Administrative Agency, National Institute of Technology and Evaluation <http://www.safe.nite.go.jp/jcheck/SearchAction?request_locale=en>

# Diisopropyl-1,1'-biphenyl[[1]](#footnote-2)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

## Persistence

The bench mark isomer with CAS No: 36876-13-8 biodegraded more than 80% in 48 hours under the River Die-Away Test using both river sediment and river water /Wemcol, 1% diisopropyl. These results indicate that the bench mark isomer is easily degraded in sediment water systems. However there is no data available for diisopropyl-1,1'-biphenyl to verify these biodegradation data.

Diisopropyl-1,1'-biphenyl cannot therefore be assessed towards the Annex D 1 (b) criteria due insufficient data.

1. **Bioaccumulation**

Only one experimental BCF identified with a value of 104721 for diisopropyl-1,1'-biphenyl. Other available bioaccumulation values are estimated also for the bench mark isomer. Since at least two experimental data points are considered as reliable for assessment towards the Annex D 1 (c) criteria, the conclusion is that there is insufficient data for this substance.

Diisopropyl-1,1'-biphenyl cannot therefore be assessed towards the bioaccumulation criteria according to Annex D 1 (c) (i) due to insufficient data.

1. **Long-range transport (LRT)**

Estimated half-life in air is 0.842 Days [AopWin v1.92]. The bench-mark diisopropylbiphenyl isomer with CAS No: 36876-13-8 is in vapor-phase degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals with a half-life of about 1 to 2 days.

Diisopropyl-1,1'-biphenyl is considered not to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

No data available in the references reviewed.

Diisopropyl-1,1'-biphenyl cannot therefore be assessed towards the Annex D 1 (e) criteria due to insufficient data.

1. **Toxicity to human health**

No data available in the references reviewed.

Diisopropyl-1,1'-biphenyl cannot therefore be assessed towards the Annex D 1 (e) criteria due to insufficient data.

 **SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [6]

|  |  |
| --- | --- |
| Common name: | Diisopropyl-1,1'-biphenyl |
| IUPAC name: | 2,2'-Diisopropylbiphenyl |
| CAS number: | 69009-90-1[[2]](#footnote-3) |
| Molecular weight: | 238.38 g/mol |
| Chemical structure: | ChemSpider 2D Image | 2,2'-Diisopropylbiphenyl | C18H22  |

1. **Chemical group**

Aromatics

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Estimated:0.0098 Pa | Epi Suite v 1.43 |
| Water solubility | Estimated:0.05528 mg/L (25°C) | Epi Suite v 1.42 |
| Partition coefficient n-octanol/water (log value) | Experimental: BCF: 104712Estimated: Log Kow : 6.67 | [1]Epi Suite v 1.68 |
| Partition coefficient air/water (log value) | Estimated: -1.195 | Epi Suite v. 1.10 |
| Partition coefficient air/octanol (log value) | Estimated: 7.865 | Epi Suite v. 1.10 |
| Henry’s Law Constant | Estimated: 1.56E-003 atm-m3/mole (25°C) |  [1] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS [6]

Regulation (EC) No 1272/2008

No harmonized classification available.

1. **Environmental fate properties**

The bench mark isomer with CAS No: 36876-13-8 biodegraded more than 80% in 48 hours under the River Die-Away Test using both river sediment and river water /Wemcol, 1% diisopropyl [2].

For the bench mark isomer diisopropylbiphenyl with CAS No: 36876-13-8, aquatic chemical reactions are not expected to play a role due to the high octanol/water partition coefficient and low water solubility of the mixture.[2].For the bench mark isomer diisopropylbiphenyl with CAS No: 36876-13-8, the highest octanol/water partition coefficient and low water solubility of the mixture indicate that they will partition into soil and sediment [2]. Based on a recommended classification scheme in the referenced study, an estimated Koc value of 160,000 (SRC[[3]](#footnote-4)), determined from a structure estimation method, indicates that diisopropylbiphenyl will be immobile in soil. Volatilization of diisopropylbiphenyl may be important from moist soil surfaces, given an estimated Henry's Law constant of 1.56E-003 atm-m3/mole (25°C), but should not be important from dry soil surfaces based on an estimated vapor pressure of 0.0098 Pa [2].

1. **Phototransformation/photolysis**

No data available.

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | 38 | Epi Suite, level III fugacity model |
| Soil  | 75 | Epi Suite, level III fugacity model |
| Sediment | 338 | Epi Suite, level III fugacity model |

1. **Potential for long range transport**

Estimated half-life in air is 0.842 Days (AopWin v1.92) Vapor-phase bench mark isomer diisopropylbiphenyl with CAS No: 36876-13-8 is degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals with a half-life of about 1 to 2 days [2].

1. **Bioaccumulation**

Only one experimental BCF with a value of 104721 has been found for diisopropyl-1,1'-biphenyl. [1]. Toxnet [2] report a calculated BCF of 69000 for diisopropylbiphenyl (CAS 36876-13-8).

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References**  |
| 1. Acute toxicity
 |  |
| No data available |  |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| No cancer classification according to IARC |  [3] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| No data available  |  |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available |  |
|  |  |
| 1. Mode of action
 |  |
| No data available |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| For the bench mark isomer diisopropylbiphenyl with CAS No: 36876-13-8 , workers were exposed to an diisopropylbiphenyl mixture, Sure Sol-250, for over 3 years in a capacitor-manufacturing plant through the inhalation of this mixture(1). Air samples taken from the breathing zone of Sure Sol-250 exposed workers contained di- and tri-isopropylbiphenyl concentrations from 0.02 to 0.05 mg/m3. No exposure doses are available. |  |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

No data available in the references reviewed.

Terrestrial compartment

No data available in the references reviewed.

1. **Other information**

A search in Scopus did not yield any peer reviewed articles with focus on health and environment for diisopropyl-1,1'-biphenyl [7] .

Diisopropyl-1,1'-biphenyl (CAS 69009-90-1) is not registered in EU (REACH).

Parts of the current assessment are based on data for an isomer (CAS No: 36876-13-8) of diisopropyl-1,1'-biphenyl that is structurally close to diisopropyl-1,1'-biphenyl (CAS No : 69009-90-1) and for which available experimental data provide a better understanding of potential characteristics of diisopropyl-1,1'-biphenyl (CAS No : 69009-90-1)

1. **References**

 [1] Chemspider, <http://www.chemspider.com/Chemical-Structure.2289772.html?rid=b36604d5-ac14-4692-8b4d-7140fba35f8f>

[2] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[3] International Agency for Research on Cancer (IARC), <http://monographs.iarc.fr/ENG/Classification/ClassificationsCASOrder.pdf>

[4] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA)., <http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[5] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[6] Harmonized Classification according to GHS Regulation (EC) No 1272/2008,

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[7] Scopus, primary literature screening search, http://www.scopus.com/home.url?zone=header&origin=resultslist

[8] ECHA registration data base
http://echa.europa.eu/information-on-chemicals

*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

# Diisoproplynaftalene (DIPN)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

## Persistence

Laboratory scale experimental data in salt and distilled water indicate that DIPN is easily degradable in water. However data from field trials provided by NITE [13] indicate that is slow with a half-life of less than 50% in 2 months in water. Thus the half-life in water exceeds the limit set out in annex D criteria of the Stockholm Convention. Since field data are considered more reliable than laboratory scale tests it is concluded that 2, 6 DINP and its isomers are not easily degraded in water under field conditions. Trials in activated sludge show a degradation rate of DIPN isomers between 20 to 50% that indicate not readily degradable in sludge. There is no data available for soil and sediment.

Diisoproplynaftalene is therefore likely to fulfil the Annex D 1 (b) (ii) criteria.

1. **Bioaccumulation**

Steady state BCF values greater than 5000 are reported for DIPN.

Diisoproplynaftalene is therefore likely to fulfil the bioaccumulation criteria according to Annex D 1 (c) (i).

1. **Long-range transport (LRT)**

Estimated half-life in air is 0.162 days [AopWin v1.92]. Half-life for the photolytic reaction in air is estimated to be 5.8 hours.

Diisoproplynaftaleneis considered not likely to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

There is one effect concentration value of LD50 in *Seriola quinqueradiata* (Yellowtail) available of approx 2 mL/kg which corresponds to high aquatic toxicity according to the GHS system. The data from NITE [13] indicate toxicities below 1 mg/L reflecting a very high toxicity to aquatic life. No ecotoxicity data was found for terrestrial compartments.

Diisoproplynaftalene is likely to fulfil the Annex D 1 (e) criteria.

1. **Toxicity to human health**

Acute toxicity LD50 exceeded 4000 mg/kg bw which indicate low acute toxicity for the substance. DIPN did not show any carcinogenic, genotoxic or reproductive toxicity effect, which suggests that DIPN is non-toxic.

Diisoproplynaftalene is not likely to fulfil the Annex D 1 (e) criteria.

**SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [4]

|  |  |
| --- | --- |
| Common name: | Diisoproplynaftalene (DIPN) |
| IUPAC name: | Bis(isopropyl)naphthalene  |
| CAS number: | 38640-62-9 |
| Molecular weight: | 212.34 g/mol |
| Chemical structure: |  **structural formula** |

1. **Chemical group**

Aromatics

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Experimental:0.00050 mm Hg (25°C)Estimated: 0.0755 Pa |  [5]Epi Suite v 1.43 |
| Water solubility | Experimental:0,11mg/L (25°C)Estimated: 0.2421 mg/L (25°C) | [5]Epi Suite v 1.42 |
| Partition coefficient n-octanol/water (log value) | Experimental:BCF: 370-3.930Estimated: Log Kow: 6.08 | [3][5]Epi Suite v 1.68 |
| Partition coefficient air/water (log value) | Estimated: -1.285 | Epi Suite v 1.10 |
| Partition coefficient air/octanol (log value) | Estimated: 7.365 | Epi Suite v 1.10 |
| Henry’s Law Constant | Estimated:1.99E-003 atm-m3/mole |  [3] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS
3. Regulation (EC) No 1272/2008

No harmonized classification available

1. **Environmental fate properties**

 Experimental data in laboratory scale for DIPN show that salt water significantly accelerated the decomposition to 70% for 2,6-DIPN. The 2,6 DIPN isomer was completely degraded after 4 h in 0.5 M NaCl solution. In distilled water however only ca. 60 % of DIPN was removed with photolytic UV irradiation. The isomer 2,7-DIPN exhibited a half-life of 6.4 h in distilled water. Half-life for naphthalene and 2-isopropylnaphthalene was 25 and 22.3 h, respectively in the same trials. [11]. In field test data provided by NITE [13], degradation showed to be low indicating a half-life to be less than 50% in 2 months in water. Biodegradation in water measured in a screening test resulted in 0 to 8% degradation of DIPN isomers in 4 weeks [13].

In a sealed vessels ready biodegradability test according to OECD test guideline 310, diisopropylnaphthalene (200 µg/L) was incubated for 56 days with activated sludge (10 mg/L SS) from a predominantly domestic sewage treatment plant. Primary degradation was followed by analysing the decrease of diisopropylnaphthalene levels in test vessels. Diisopropylnaphthalene was analysed by a GC-method measuring seven individual diisopropylnaphthalene isomers (individual GC peaks). Degradation was measured on day 4, 8, 14, 21, 28, 40, and 56.
Total primary degradation of diisopropylnaphthalene was ca. 50% within the test period. 20 to 30% was caused by abiotic degradation. Primary biodegradation was found to be about 20 to 30% for all isomers. There appeared no relevant increase in overall biodegradation from day 21 to day 56 (varying levels of biodegradation between 20 to 30%) [11].

Distinct diisopropylnaphthalene isomers showed variable biodegradation. For three isomers, no primary biodegradation could be demonstrated. For four isomers, 15 to 100% primary biodegradation was noted at the end of the test period. Abiotic degradation was similar for all isomers within certain variations. Between day 14 and 40, abiotic biodegradation seemed to level off at around 15 to 20%. On day 56, rates of around 30 to 35% abiotic primary degradation was observed [11].

The biodegradation of (14)C-labelled diisopropylnaphthalene with activated sludge was studied. In high concentration of (14)C-labelled diisopropylnaphthalene (10 ppm), the biodegradation was slow, with approximately 35% of diisopropylnaphthalene evoluted to (14)C-carbon dioxide (CO2) after 4 weeks(1). In a low concentration (0.4 ppm), (14)C-labelled diisoprpylnaphthalene was degraded much faster and (14)C-carbon dioxide evolved reached to about 80% in 4 weeks. Both side chain (isopropyl group) and naphthalene nucleus could be attacked in biodegradation, since propionic acid and salicyclic acid derivatives were found as the metabolites. In a 4-week biodegradation screening test (MITI test) using diisopropylnaphthalene (30 mg/L) and an activated sludge inoculum (100 mg/L), 0% of theoretical BOD was removed [5].

1. **Phototransformation/photolysis**

According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere, diisopropylnaphthalenes (SRC[[4]](#footnote-5)), which have a vapor pressure of 0.00050 mm Hg at 25°C, is expected to exist primarily as a vapor in the ambient atmosphere. Vapor-phase diisopropylnaphthalenes are degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals. From photolytic degradation of 2-isopropylnaphthalene, four photolysis products were identified: 2-(2-naphthyl)-2-propanol, phthalide, benzoic acid and phthalic acid [11].

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | < 4 h (salt water)< 6.5 h (distilled water)38 | [11]Epi Suite, level III fugacity model |
| Soil  | 75 | Epi Suite, level III fugacity model |
| Sediment | 338 | Epi Suite, level III fugacity model |

1. **Potential for long range transport**

Estimated half-life in air is 0.162 days (AopWin v1.92)

Half-life for the photolytic reaction in air is estimated to be 5.8 hours, calculated from its rate constant of 6.6x10-11 cm3/molecule-sec at 25°C that was derived using a structure estimation method. Diisopropylnaphthalenes may absorb light with wavelengths >290 nm, and may be susceptible to direct photolysis by sunlight [5].

1. **Bioaccumulation**

 One study suggests measured BCF in the range of 370-3930 in aquatic organisms [5].

The extent of bioaccumulation, according to the OECD Guideline 305 test method, is dependent on individual components (isomers). The extent of bioaccumulation is also dependent on the exposure concentration. At the low concentration, the BCF was significantly lower (highest value 2400) compared to the high concentration (highest value 6400) [11]. The Japanese NITE database report BCFs for diisopropylnaphthalene (DIPN) of 3500 and 7000 in common carp, which is lower than the values they report for triisopropylnaphthalene [13]. Furthermore, the estimated logKow of 6.08 also meets the criteria.

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References** |
| 1. Acute toxicity
 |  |
| LD50 Mouse oral 5100 mg/kgLD50 Mouse percutaneous 4600 mg/kg | [11] |
|  |  |
| 1. Carcinogenity and Mutagenicity
 |  |
| 1. DIPN did not show any carcinogenic potential up to the highest dose tested.
 | 1. [11]
 |
| No cancer classification according to IARC | [6] |
| 1. In an *in-vitro* mammalian chromosome aberration test, diisopropylnaphthalene did not demonstrate any increase in chromosomal damage at any dose level either without or with metabolic activation. There was no evidence of any clastogenic activity under the conditions of the test used.
2. The mutagenic potential of diisopropylnaphthalene (DIPN) was tested in an in-vitro mammalian cell gene mutation assay using mouse lymphoma L5178Y cells. There was no evidence of increases in mutant frequency according to the criteria of the test for all test substance concentrations tested without and with metabolic activation. It can be concluded that DIPN does not demonstrate mutagenic potential under the test conditions of this assay.
 | 1. [11]
 |
|  |  |
| 1. Toxicity for reproduction
 |  |
| The treatment of pregnant rats produced no pathologically relevant effects, neither in the dams nor in the offspring. No particular pathological finding in the fetuses and in pups during lactation and after weaning | [11] |
| Diisopropylnaphthalene was administrated orally to pregnant mice on 7th-12th days of pregnancy at 192 or 19.2 mg/kg. No effects were observed on litter size, nidation number, sex ratio, & skeleton of fetuses for primary & secondary parents. | [5] |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available |  |
|  |  |
| 1. Mode of action
 |  |
| Subchronic or Prechronic Exposure/ The effects of diisopropylnaphthalenes (KMC) and 1-phenyl-1-xylylethanes (SAS) were examined in rats. The rats were administered 0.1 g of the substances/kg bw every day for 1 month. The substances were given directly into the stomach with a syringe. At 2 hr after receiving the final dosage, the rats were killed and examined biochemically. An increase in liver weight, disturbance of lipid metabolism in the liver and serum and disturbance of glucose metabolism in the liver were observed.  | [5] |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| NIOSH (NOES Survey 1981-1983) has statistically estimated that 2087 workers (13 of these are female) are potentially exposed to diisopropylnaphthalenes in the US(1). Occupational exposure to diisopropylnaphthalenes may occur through inhalation and dermal contact with this compound at workplaces where diisopropylnaphthalenes are produced or used(SRC). Monitoring data indicate that the general population may be exposed to diisopropylnaphthalenes via ingestion of food, and dermal contact with this compound and products containing diisopropylnaphthalenes. However no acceptable exposure limits are available. | [5] |
|  |  |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

1. There is one effect concentration value of LD50 in Seriola quinqueradiata (Yellowtail) ip available of approx 2 mL/kg [5] which corresponds to high aquatic toxicity according to the GHS system. The NITE database report toxicity results for algae, daphnia and fish (Oryzias latipes). EC50s from these experiments are >0.071 mg/L, 0.035 and > 0.093 mg/L respectively [13].

Terrestrial compartment

No data available in the references reviewed

1. **Other information**

A search in Scopus yielded 1 peer reviewed articles with focus on health and environment for diisoproplynaftalene [10]**.**

The EU PBT Working Groupconcluded that individual isomers of DIPN meet at least the B criterion and on available data concluded that DIPN fulfilled the T-criterion. However it cannot be precluded that some of the DIPN isomers may fulfil the P or even the vP-criterion of Annex XIII of REACH [14].

1. **References**

[1] IUCLID, <http://esis.jrc.ec.europa.eu/doc/IUCLID/data_sheets/38640629.pdf>

[2] ESIS, <http://esis.jrc.ec.europa.eu/doc/PBT-evaluation/PBT_sum125_CAS_38640-62-9.pdf>

[3] OECD, <http://webnet.oecd.org/CCRWEB/ChemicalDetails.aspx?ChemicalID=5bbb30fa-beb8-4c8a-941c-1e8f8bb1c8c3>

[4] Chemspider, <http://www.chemspider.com/Chemical-Structure.2289772.html?rid=b36604d5-ac14-4692-8b4d-7140fba35f8f>

[5] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[6] International Agency for Research on Cancer (IARC), <http://monographs.iarc.fr/ENG/Classification/ClassificationsCASOrder.pdf>

[7] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA)., <http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[8] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[9] Harmonized Classification according to GHS Regulation (EC) No 1272/2008,

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[10] Scopus, primary literature screening search, <http://www.scopus.com/home.url?zone=header&origin=resultslist>

[11] ECHA registration data base.
<http://echa.europa.eu/information-on-chemicals>

*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

[12] Motoharu Suzuki & Chisato Matsumura & Takeshi Nakano & Hiromasa Imaishi, “Investigation of environmental contamination of mono-isopropylnaphthalene, di-isopropylnaphthalene and tri-isopropylnaphthalene in Hyogo in Japan”, Environ Sci Pollut Res, DOI 10.1007/s11356-012-0987-9 (2012), http://ee-net.ne.jp/serbia/paper/suzuki-DIPN.pdf

[13] Nite, Incorporated Administrative Agency, National Institute of Technology and Evaluation <http://www.safe.nite.go.jp/jcheck/SearchAction?request_locale=en>

[14] The EU PBT Working Group transitional DIPN assessment report (2012)

# Dodecamethyl cyclohexasiloxane (D6)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

* 1. **Persistence**

A number of studies report half-life values of more than 60 days in water for D6. Degradation of D6 in soil depends on the water content, being higher in humid soils. No experimental data are available for persistence in sediment.

D6 is therefore considered to fulfil the persistence criteria according to Annex D 1 (b) (i).

* 1. **Bioaccumulation**

Several empirical bioconcentration factors (BCF) of less than 2500 have been reported.

D6 is therefore considered not to fulfil the bioaccumulation criteria according to Annex D 1 (c) (i).

* 1. **Long-range transport (LRT)**

D6 has the potential to be transported over long-distances in the atmosphere. In air, D6 is persistent with calculated atmospheric half-lives of more than 2 days. Estimations of the transport distance and monitoring data also indicate that D6 can be transport over long distances.

D6 is therefore considered to fulfil the Annex D 1 (d) (iii) criteria.

* 1. **Ecotoxicity**

The experimental toxicity data showed no adverse effects to pelagic aquatic organisms at concentrations up to 0.0046 mg/L, its approximate water solubility limit. Given the low bioavailability, and low potential for effects, it is concluded that D6 has low potential to cause ecological harm in the aquatic and terrestrial environment.

D6 is therefore not likely to fulfil the Annex D 1 (e) (i) criteria.

* 1. **Toxicity to human health**

D6 exhibits low acute toxicity, with LD50 values > 2000 mg/kg body weight. D6 has not been classified by IARC for carcinogenicity, genotoxicity or reproductive/developmental toxicity. Data on the endpoints for carcinogenity, genotoxicity and reproductive/developmental toxicity are negative. Environment Canada estimated a margin of exposure of approximately 40.000 between the critical effect level for repeated dose and the upper bound estimate for daily intake. Therefore D6 is considered not to be toxic to humans.

D6 is therefore not likely to fulfil the Annex D 1 (e) (ii) criteria.

 **SUMMARY OF DATA**

* 1. **Identity of the substance and physical and chemical properties**
1. **Name and other identifiers of the substance**

Table 1: Substance identity [2]

|  |  |
| --- | --- |
| Common name: | Dodecamethyl cyclohexasiloxane (D6) |
| IUPAC name: | Dodecamethylcyclohexasiloxane  |
| CAS number: | 540-97-6 |
| Molecular weight: | 444.93 g/mol |
| Chemical structure: | ChemSpider 2D Image | DODECAMETHYLCYCLOHEXASILOXANE | C12H36O6Si6 |

1. **Chemical group**

Cyclic volatile methyl-siloxanes (cVMS)

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

| **Property** | **Value** | **References** |
| --- | --- | --- |
| Vapour pressure | Experimental4.6 Pa(0.0345 mm Hg) Estimated:4.73 Pa(0.0355 mm Hg)  | [1] |
| Water solubility (mg/L) | Experimental and estimated: 0.005  |  [1] |
| Partition coefficient n-octanol/water (log value) | Experimental:5.86 to 9.06Estimated: 9.08 |  [1]Epi Suite v 1.10 |
| Partition coefficient air/water Partition coefficient (log value) | 8.427 | Epi Suite v 1.10 |
| Partition coefficient air/octanol (log value) | 8.427 | Epi Suite v 1.10 |
| Henry’s Law Constant | Experimental:14 667 (0.145 atm·m3/mol) 6712 (0.066 atm·m3/mol) Estimated:16 212 (0.16 atm·m3/mol)  |  [1][1][1] |

* 1. **Classification and labelling**
1. Harmonized Classification according to GHS [3]

Regulation (EC) No 1272/2008 –

No harmonized classification available.

* 1. **Environmental fate properties**

 A half-life of ~401 days was extrapolated for D6 based on the experimental hydrolysis half-lives of D4 and D5 at neutral pH and ambient temperature. D6 is therefore considered persistent under typical Canadian water conditions [1].

 A biodegradation result of 4.47% in 28 days in water was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. An amount of the test substance may have been present in headspace of test vessels and therefore not available for biodegradation [10].

A 28-day ready-biodegradability test was performed in sealed vessels in accordance with OECD Draft Guideline 310; data showed limited biodegradation (4.47%) of D6, indicating a probability of biodegradation of D6 in water of effectively zero [8].

Half-lives in temperate soil of 158 to 202 days (depending on relative humidity) and in tropical soil of 1.8 to 3.0 days (depending on relative humidity) were obtained using accepted calculation methods. The results are considered to be reliable [10].

In air-dried soils, further hydrolysis of dimethyl siloxanes to dimethylsialanediol occured in a few hours up to 1 week depending on humidity [8].

A degradation half-life on Wahiawa soil of 1.38 days was determined in a reliable study conducted according to an appropriate test protocol [10].

In sediment dimethyl siloxanes are estimated to be persistent, but no experimental data have been found [10].

* 1. **Phototransformation/photolysis**

Vapor-phase **D6** is degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals [8].

* 1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | Experimental. >411 | [1] |
| Soil  | 1.38 - 202Estimated:< 182 | [10][1] |
| Sediment | Estimated:>365 | [1] |

* 1. **Potential for long range transport**

D6 has the potential to be transported over long-distances in the atmosphere. In air, D6 is persistent with calculated atmospheric half-live of 5.958 Days [.AopWin v1.92]. Wang [9] summarizes literature data, and state “Excellent agreement between the model predictions and field observations indicate that cVMS have high LRAT potential.” The long range transport ability of D6 is confirmed by monitoring data which show that cyclic siloxane concentrations in air from the background and Arctic sites decrease in the order of D4 > D5 > D6. Transport distance of D6 cited in Wang et al. [9] is 2966 km.

* 1. **Bioaccumulation**

The public available data in the REACH registration (ECHA, 2014) report BCFs of 1160, 1660 and 2400 [10].

Steady-state BCF value of 1160 and kinetic BCF value of 1660 in fathead minnows (Pimephales promelas) were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. Taking into account that 79% of the radioactivity in the fish was parent compound, it can be estimated that the BCF based on parent compound alone would be ≥916 L/kg [10].

The steady-state BCF in Daphnia magna of approximately 2400 was determined in a reliable study conducted according to generally accepted scientific principles [10].

 Reported BMF and TMF were smaller than unity, whereas BAFs reported were 0.66 and 0.70. Similar data are provided in document on D6 by Environment Canada (2008), which also report one modelled BAF value that is higher than 5000. Environment Canada (2008) attributes the low experimental BCF to the limited aquatic bioavailability compared to D4 and D5. The empirical and modelled log Kow values for D6 (Table 2) suggest that this substance has the potential to bioaccumulate in biota. On the estimated BAF larger than 5000 Environment Canada (2008) indicates that the estimate has a certain degree of uncertainty.

* 1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References** |
| 1. Acute toxicity
 |  |
| The LD50 value of >2000 mg/kg bw was determined in a reliable study conducted according to an appropriate protocol, and in compliance with GLP. The LD50 value of >2000 mg/kg was determined in a reliable study conducted according to an appropriate test protocol and in compliance with GLP. | [10] |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| No cancer classification according to IARC | [4] |
| No carcinogenicity data for D6 were identified.Results of mutagenicity assays using *Salmonella typhimurium* or *Escherichia coli* (NOTOX 1990c) were negative. Dodecamethylcyclohexasiloxane (D6) has been tested in a reliable in vivo micronucleus assay in ICR mice conducted according to OECD TG 474 and in compliance with GLP. No statistically significant increase in the incidence of micronucleated polychromatic erythrocytes relative to control was observed in any test substance group up to limit concentrations at 24 and 48 hours after intraperitoneal administration of the test substance. Reductions in PCE/EC ratio (up to 11%) were observed in some test article groups, indicating that the test article had reached the target tissue. Administration of cyclophosphomide (the positive control) induced marked increases in micronucleated polychromatic erythrocytes. It is concluded that the test substance is negative for the induction of micronuclei in vivo under the conditions of the test. | [1][10] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| With regard to reproductive toxicity, a lowest-observed-effect level (LOEL) of 1000 mg/kg-bw/day was determined based on an increased number (non-statistical) of sperm-positive, non-gravid females in a repeated-dose reproductive and developmental toxicity study. A well reported oral combined repeated dose/reproductive and developmental toxicity study in the rat, conducted according to the current guideline and in accordance with GLP, identified an NOAEL of 1000 mg/kg bw/day for reproductive effects. This screening study found that the increased number of non-gravid females at this dose was not statistically significant. There was no evidence of this effect at the lower dose of 330 mg/kg bw/day. | [1][10] |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available  |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available  |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available  |  |
|  |  |
| 1. Mode of action
 |  |
| No data available  |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| The critical effect level for repeated-dose toxicity is considered to be 100 mg/kg-bw/day via the oral route. This is based on increased liver weights in a 90-day rat study, as well as the extrapolation of critical effects and levels from oral data on the similar compounds D4 and D6 to D5.  | [1] |

* 1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

The experimental toxicity data showed no adverse effects to pelagic aquatic organisms at concentrations up to 0.0046 mg/L, its approximate water solubility limit. However, reduced bioavailability compared to its close analogues, D4 and D5, suggests that no toxic threshold for adverse effect is expected for D6 at its water solubility limit. [1]

A 28-Day EC50 value of 37 mg/kg dry weight has been determined for the effects of the sediment incorporated test substance on mortality of Chironomus riparius. A NOEC of <22 mg/kg dry weight for effects on development rate and development time has been determined in the same test [10].

A 28-d EC50 value of >420 mg/kg dry weight and a NOEC of ≥420 mg/kg dry weight have been determined for the effects of the test substance on numbers and biomass of Lumbriculus variegatus recovered from treated sediments. The results are expressed relative to mean measured exposure concentrations [10].

Information on the toxicity of D6 to sediment-dwelling organisms is not available; a conservative read-across from D5 was applied and it is concluded that the no-effect concentration for D6 to the benthic community is above 69 mg/kg [10].

Terrestrial compartment

A 28-day LC50 value of >4074 mg/kg dry weight and a 56-day NOEC of ≥4074 mg/kg dry weight have been determined for the effects of the test substance on mortality and reproduction and growth respectively of Eisenia andrei [10].

A 28-day LC50 value of 813 mg/kg dry weight and a 28 day IC50 value of 767 mg/kg dry weight have been determined for the effects of the test substance on mortality and reproduction of Folsomia candida. A NOEC of 377 mg/kg dry weight has been determined by the reviewer on the basis of a visual examination of the data for both mortality and reproduction [10].

* 1. **Other information**

A search in Scopus yielded 6 peer reviewed articles with focus on health and environment for D6 [6].

Environment Canada concluded that, given the low bioavailability and low potential for effects, D6 has low potential to cause ecological harm and does not meet the legal definition of toxic. It is concluded that D6 meets the criteria for persistence as set out in the Persistence and Bioaccumulation Regulations. However, D6 does not meet the criteria for bioaccumulation [1].

* 1. **References**

[1] Environment Canada Health Canada , Screening Assessment for the Challenge, Dodecamethyl cyclohexasiloxane (D6), (2008), <http://www.ec.gc.ca/ese-ees/FC0D11E7-DB34-41AA-B1B3-E66EFD8813F1/batch2_540-97-6_en.pdf>

[2] Chemspider, [http://www.chemspider.com](http://www.chemspider.com/Chemical-Structure.10451.html)

[3] Harmonized Classification according to GHS Regulation (EC) No 1272/2008

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[4] International Agency for Research on Cancer (IARC)

<http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[5] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[6] Scopus, primary literature screening search, http://www.scopus.com/home.url?zone=header&origin=resultslist

[7] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[8] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[9] Wang, De-Gao, et al. "Review of recent advances in research on the toxicity, detection, occurrence and fate of cyclic volatile methyl siloxanes in the environment." *Chemosphere* Vol. 93, Issue 5, October 2013: 711–725

[10] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

# 1-Isopropyl-2-phenyl-benzene

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other

hazard indicators

1. **Persistence**

Experimental data on biodegradation in water and sediment -water samples suggest a rapid degradation of similar monoisopropyl biphenyl isomers. The substances were completely degraded in sediment-water samples within one week that suggest half-life in water and sediment much less than 2 month and 6 month respectively.

1-Isopropyl-2-phenyl-benzene is considered not to fulfil the Annex D 1 (b) criteria for persistence.

1. **Bioaccumulation**

In an experimental study, BCF were determined to be 2896 and 10790 respectively. Two experimental log Kow values are available namely 5.33 and 5.51.

1-Isopropyl-2-phenyl-benzene is considered to fulfil the Annex D 1 (c).

1. **Long-range transport (LRT)**

Estimated half-life in air is 1.098 Days [AopWin v1.92]. Vapor-phase isopropylbiphenyl is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, the half-life for this reaction in air is estimated to be about 40 hours, a bit less than 2 days.

1-Isopropyl-2-phenyl-benzene is therefore considered not to fulfil the Annex D 1 (d) (iii) criteria

1. **Ecotoxicity**

The substance is suggested with the data available to show high toxicity to aquatic organisms. There was no data available for terrestrial organisms.

1-Isopropyl-2-phenyl-benzene is likely to fulfil the Annex D 1 (e) criteria.

1. **Toxicity to human health**

The substance show acute toxicity data of more than 5000 mg/kg bw and is therefore considered non-toxic. No cancer classification according to IARC. Mutagenicity tests are negative .There are no data available for any other toxicity endpoints.

1-Isopropyl-2-phenyl-benzene is not likely to fulfil the, the Annex D 1 (e) criteria.

 **SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [1]

|  |  |
| --- | --- |
| Common name: | 1-Isopropyl-2-phenyl-benzene |
| IUPAC name: | (1-methylethyl)-1,1'-biphenyl  |
| CAS number: | 25640-78-2 |
| Molecular weight: | 196.29 g/mol |
| Chemical structure: | structural formula |

1. **Chemical group**

Aromatics

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Experimental: 0.4993 Pa (20°C)0.7623 Pa (25°C)1.1475 Pa (30°C)Estimated: 0.109 Pa (25°C) | [8][8][8]Epi Suite v 1.43 |
| Water solubility | Experimental: 0.482 mg/L (25°C)Estimated: 1,656 mg/L (25°C) | [8] Epi Suite v 1.42 |
| Partition coefficient n-octanol/water (log value) | Experimental: 5.33 and 5.51  | [8] |
| Partition coefficient air/water (log value) | Estimated: -2.056 | Epi Suite v.1.10 |
| Partition coefficient air/octanol (log value) | Estimated: 7.256 | Epi Suite v. 1.10 |
| Henry’s Law Constant | Estimated: 8.05E-004  | [1] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS

Regulation (EC) No 1272/2008 [2]

No harmonized classification available.

1. **Environmental fate properties**

 A monoisopropyl biphenyl isomer mixture (MIPB) was rapidly biodegradable under aerobic conditions in the mineralisation (Headspace test (OECD 310). The criteria for "ready biodegradability" were not fully met: about 58 % CO2 (28 d) with a time window of about 20 days (instead of 10 days). But based on a time-decomposition curve considered to be readily biodegradable [8].

In a pre-guideline BOD die-away test following the basic procedure of OECD TG 301D, isopropylbiphenyl was demonstrated to undergo biodegradation. The concentration of isopropylbiphenyl in the test was 0.184 mg/L and the inoculum was sampled from an industrial wastewater treatment plant. But due to the low initial concentration used along with the low number of replicates, no firm conclusion can be drawn from O2 consumption in a quantitative meaning for ultimate degradation [8].

More than 80% of the added isopropylbiphenyl biodegraded aerobically within 48 hr in a sediment-water sample using the River Die-Away Test. In sewage sludge tests, isopropylbiphenyl was biodegraded 60% in 24 hours and completely biodegraded within one week [7].

1. **Phototransformation/photolysis**

Vapor-phase isopropylbiphenyl is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be about 40 hours [7].

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | 38 | Epi Suite, level III fugacity model |
| Soil  | 75 | Epi Suite, level III fugacity model |
| Sediment | >80% degraded in 2 days338 | [7]Epi Suite, level III fugacity model |

1. **Potential for long range transport**

Estimated half-life in air is 1.098 Days (AopWin v1.92). The half-life for the formation of hydroxyl radicals in air is estimated to be about 40 hours [7].

1. **Bioaccumulation**

In a flow-through bioconcentration test with flagfish similar to OECD TG 305E (May 1981), two different concentrations of isopropylbiphenyl were applied (measured 3.5 and 24.1 µg/L). BCF values were calculated by division of uptake and depuration rate constants determined from measured concentration data using the computer program BIOFAC. BCF were determined to be 2896 and 10790 respectively [7][8]. Two experimental log Kow values are available: 5.33 and 5.51 [8]. Model estimations provided in the REACH dossier result in BCF values smaller than 5000 [8].

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References**  |
| 1. Acute toxicity
 |  |
| LD50 Rat oral 4.7 g/kg /SURE SOL 250, 6% di- and triisopropyl/ | [7] |
| LD50 Rat Oral 8.5 g/kg /SURE SOL 250, 6% di- and triisopropyl | [7] |
| Inhalation of 20.8 mg/L by 10 rats for 1 hr at 18-20 deg C produced no deaths. Grooming and slight depression were observed during and immediately following exposure. Autopsy revealed no gross anomalies | [7] |
| In a 28-day pilot feeding study with rats using various concentrations, there was no indication of adverse effects at levels as high as 0.1%. /Wemcol1, 1% diisopropyl/ | [7] |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
|  |  |
| No cancer classification according to IARC | [3] |
| Mutagenicity test item was negative in the mouse lymphoma forward mutation assay both with and without S9 metabolic activation under the conditions of testing. | [8] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| No data available  |  |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available |  |
|  |  |
| 1. Mode of action
 |  |
| No data available |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| Complaints of an unpleasant smell, headaches, irritation, fatigue and redness of the face and eyes were reported in female office workers handling self- copying paper forms. The smell was attributed to the release of isopropyl biphenyl solvent. Office workers indicated only eye, and respiratory tract irritation caused by carbonless copy paper containing this chemical was most often associated with symptoms. It is a mild irritant on abraded skin, slight irritant on intact skin. Acceptable exposure dose is not available. | [7] |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

In a valid short-term toxicity test to daphnia, a 48-h EC50 of 0.24 mg/L was determined [9].

LC50 Bluegill sunfish static 4 mg/L 96hr /Wemcol**[[5]](#footnote-6)**, 1% diisopropyl/LC50 Rainbow trout 2.5 mg/L 96 hr static /Wemcol, 1% diisopropyl/[7]

LC50 Flagfish (adult) > 0.75 mg/L 96hr flow-through /Wemcol, 1% diisopropyl/[7]

LC50 Flagfish (fry) 0.28 mg/L 96 hr flow-through /Wemcol, 1% diisopropyl/[7]

Threshold spawning impairment flagfish > 0.42 mg/L 21 day /Wemcol, 1% diisopropyl[7]

Threshold hatching impairment flag fish > 0.47 mg/L /21 day. /Wemcol, 5% di- and triisopropyl/[7]. The data indicate that 1-Isopropyl-2-phenyl-benzene should be considered as highly toxic to aquatic organisms.

Terrestrial compartment

No data available in the references reviewed

1. **Other information**

A search in Scopus yielded 2 peer reviewed articles with focus on health and environment for 1-Isopropyl-2-phenyl-benzene [5].

1. **References**

[1] Chemspider, http://www.chemspider.com/

[2] Harmonized Classification according to GHS Regulation (EC) No 1272/2008

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[3] International Agency for Research on Cancer (IARC)

<http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[4] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[5] Scopus, primary literature screening search, <http://www.scopus.com/home.url?zone=header&origin=resultslist>

[6] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[7] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[8] ECHA registration data base\*.
http://echa.europa.eu/information-on-chemicals*\*Note:primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

# Octamethyl cyclotetrasiloxane (D4)

***Overall conclusion: Class 1: Substances that are likely to meet all Annex D criteria (b), (c), (d) and (e)***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

1. **Persistence**

A biodegradation rate of 3.7% in 29 days in water indicates that D4 has a half-life in water greater than 2 month. Data available on the degradation of D4 in sediment show that it has a relatively long half-life, of the order of 242 days at 24°C under aerobic conditions, and 365 days at 24°C under anaerobic conditions. However D4 half-life in soil is dependent on the %RH value.

D4 is considered to fulfil the persistence criteria according to Annex D 1 (b) (i).

1. **Bioaccumulation**

The steady state BCF for D4 has been determined as 12,400 L/kg in fathead minnows

There are also empirical log Kow data that range between 4.34 to 6.49 for D4 [11].

D4 is therefore considered to fulfil the bio-accumulation criteria according to Annex D 1 (c) (i).

1. **Long-range transport (LRT)**

The half-life of D4 in the atmosphere is estimated to be about 14 days.

Therefore D4 is therefore considered likely to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

The European Commission has classified D4 as a Hazardous to the aquatic environment (Aquatic Chronic 4) [5]. Considering D4’s potential to bioaccumulate in biota and its toxicity to sensitive aquatic organisms, long-term environmental exposure may cause adverse effects to aquatic organisms.

Therefore D4 is likely to fulfil the Annex D 1 (e) (i) criteria.

1. **Toxicity to human health**

The European Commission has classified D4 as a reproductive toxic substance (repr. 2) (H361f) [5].

D4 is therefore likely to fulfil the Annex D 1 (e) (ii) criteria

**SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [3]

|  |  |
| --- | --- |
| Common name: | Octamethyl cyclotetrasiloxane  |
| IUPAC name: | 2,2,4,4,6,6,8,8-Octamethyl-1,3,5,7,2,4,6,8-tetroxatetrasilocane |
| CAS number: | 556-67-2 |
| Molecular weight: | 296.2 g/mol |
| Chemical structure: | ChemSpider 2D Image | Octamethylcyclotetrasiloxane | C8H24O4Si4 |

1. **Chemical group**

Cyclic volatile methyl-siloxanes (cVMS)

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Experimental: 140 Pa(1.05 mm Hg, at 25°C.)132 Pa(0.99 mm Hg at 25°C.)Estimated:157.3(1.18 mm Hg at 25°C) |  [1] |
| Water solubility | Experimental:0.0562 mg/L at 23°C0.074 mg/L (freshwater) 0.033 mg/L (saltwater)Estimated:0,05 mg/L at 25°C | [1]  |
| Partition coefficient n-octanol/water (log value) | Experimental:6.49 Estimated:6.74 | [11]Epi Suite v 1.68 |
| Partition coefficient air/water (log value) | Experimental:2.69 at 21,7°C | [11] |
| Partition coefficient air/octanol (log value) | 0.680 |  [3] |
| Henry’s Law Constant | Experimental:1 220 000 (Pa·m3/mol)(12.0 atm·m3/mol) 11898 (Pa·m3/mol) at 25°C(0.117 atm·m3/mol)60060 (Pa·m3/mol) at 28°C(0.593 atm·m3/mol)57558 (Pa·m3/mol) at 28°C(0.568 atm·m3/mol)Estimated:9119.3 (Pa·m3/mol) at 25°C(0.09 atm·m3/mol) | [1] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS [5]

Regulation (EC) No 1272/2008

|  |  |
| --- | --- |
| **Classification** | **Hazard statement** |
| Repr. 2 | H361f |
| Aquatic Chronic 4 | H413 |

1. **Environmental fate properties**

A biodegradation result of 3.7% in 29 days in water was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [12].

New data available on the degradation of D4 in sediment show that it has a relatively long half-life, of the order of 242 days at 24°C under aerobic conditions, and 365 days at 24°C under anaerobic conditions. The half-life at lower temperatures (e.g. 12°C) would be expected to be longer. The sediment half-life appears to depend on the sediment characteristics (e.g. pH and organic carbon content); for example, a half-life of 47 days at 24°C (equivalent to a half-life of 123 days at 12°C) was found in a second sediment [12].

A sediment degradation half-life of 365 days at 24°C and under anaerobic conditions was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. The major degradation products were hydrolytic products, such as dimethylsilandiol and non-extractable silanols, while 14C-CO2 generation and 14C-methane generation is minimal, indicating complete mineralisation of D4 or its degradation products is very slow [12].

D4 degradation in non-sterilised samples was almost the same as that in the chemically sterilised samples, suggesting that the degradation of D4 in the sediment under anaerobic conditions may be predominantly abiotic [12].

D4 was found to hydrolyse rapidly in air-dried Wahiawa soil and air-dried Londo, in closed tubes at ~22°C in the dark, to form degradation intermediates (oligomeric diols) in a reliable study conducted according to generally accepted scientific principles. Given sufficient time, these degradation intermediates ultimately hydrolysed to dimethylsilanediol. Half-lives on Wahiawa soil of 0.04 to 0.89 days (dependent on relative humidity (RH)) and on Londo soil of 3.54 and 5.25 days (dependent on RH) were determined [12].

The degradation seen was thought to be the result of hydrolysis reactions catalyzed by the surface activity of soil clays.

The hydrolysis rate decreased with an increase in RH. This was thought to be due to decreased surface acidity and thus the hydrolysis rate at higher RH. The degradation half-lives in Wahiawa soil were: 0.04 days (32% RH); 0.08 days (92% RH); 0.89 days (100% RH). The degradation half-lives in Londo soil were: 3.54 days (32% RH); 5.25 days (92% RH) [12].[Legal](http://echa.europa.eu/web/guest/legal-notice)

1. **Phototransformation/photolysis**

D4 is not expected to react, or react appreciably, with other photo-oxidative species in the atmosphere, such as O3; nor is it likely to degrade via direct photolysis). Therefore, it is expected that reactions with hydroxyl radicals will be the most important fate process in the atmosphere for this substance. Thus, it may be concluded that the degree to which aerosols and ozone accelerate degradation of cVMS in air under realistic environmental conditions is uncertain [1].

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | Experimental. >>29  |  [12] |
| Soil  | Experimental.0.04 to 5.2 depending on %RH  |  [12] |
| Sediment | Experimental. 242 - 365 |  [12] |

1. **Potential for long range transport**

The degradation half-life of D4 in the atmosphere is estimated to be around 14 days, although the half-life may be shorter in urban and suburban areas. Thus volatilisation followed by subsequent degradation in the atmosphere is an important process in the overall persistence of D4 in the environment [12].

1. **Bioaccumulation**

A steady-state BCF value of 12400 and kinetic BCF value of 13400 were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [12].

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References** |
| 1. Acute toxicity
 |  |
| An acute oral LD50 value of >5mL/kg (ca. 4800 mg/kg) was determined in a reliable study conducted according to an appropriate test protocol. Not conducted according to GLP. | [12] |
| An acute inhalation LC50 value of 36 mg/L air was determined in a reliable study conducted according to an appropriate protocol, and in compliance with GLP. | [12] |
| An acute dermal LD50 value of >2500 mL/kg was determined in a reliable study conducted according to an appropriate test protocol. Not conducted according to GLP. | [12] |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| No cancer classification according to IARC. | [6] |
| The NOAEL for carcinogenic effects was 150 and ≥700 ppm in females and males, respectively. | [12] |
| For mutagenicity octamethylcyclotetrasiloxane has been tested in mouse lymphoma L5178Y cells in a valid study that was similar to OECD 476, but not in compliance with GLP. The test did not cause a statistically significant increase in mutation, and is therefore non-mutagenic in L5178Y mouse-lymphoma cells. | [12] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| The European Commission has classified D4 as a repr. 2 (H361f) through the CLP regulation. | [5] |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available  |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available  |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available in the studies reviewed |  |
|  |  |
| 1. Mode of action
 |  |
| No data available  |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| Although the focus of the assessment by the European Commission was inhalation, the DanishEPA assessment did not distinguish between exposure routes. Thus, it is considered prudent toestablish a critical effect level for oral exposure, as a limited amount of oral toxicity data wasavailable. As stated above, the critical effect level for repeated-dose toxicity is considered to be100 mg/kg-bw/day via the oral route. This is based on decreased serum estradiol in the 7-daymouse studies and decreased body weights and relative liver weights in fetuses in 8-day ratstudies (D4 administered to pregnant females). | [1] |
| Comparison of the critical effect dose level for repeated dosing via the oral route(100 mg/kg-bw/day) and the upper-bounding estimate of daily intake ofoctamethylcyclotetrasiloxane by the general population in Canada results in a margin of exposure of approximately 5800. This is based on adjusting the inhalation contribution to daily intake by an inhalation absorption value of 12%, resulting in a systemic exposure of 17.3 μg/kg-bw/day. | [1] |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

The European Commission has classified D4 as a Hazardous to the aquatic environment (Aquatic Chronic 4) [1].

A short term 96-hour LC50 of >22 µg/L has been determined for the effects of the test substance on mortality of Oncorhynchus mykiss. A NOEC of ≥22 µg/L has been determined in the same test. 14-day LC50 and NOEC values reported in the test were 10 and ≤4.4 µg/L respectively. However the NOEC can be concluded to be 4.4 µg/L because mortality effects at this loading level, the lowest loading level and in the control were equal [12].

A long-term NOEC for water exposure of fish is ≥4.4 μg/L from a long-term (93-day) toxicity study with Oncorhynchus mykiss(this was the highest concentration tested in the study and no adverse effects were observed). However, a 14-day NOEC with the same species also gave a NOEC of 4.4 μg/L: although normally considered to be a prolonged acute toxicity test, this is consistent with the limit NOEC obtained in the 93-day fish early life stage study and so the overall NOEC for fish is assumed to be around 4.4 μg/L. It is noted that this substance has effects on mammalian reproduction (see below), and no data are available to determine whether it affects fish reproduction [12].

D4 is not toxic to aquatic invertebrates when they are exposed for short durations up to 96 hours at concentrations up to the water solubility limit. Following longer exposure toxicity is apparent and the long-term (21-day) NOEC for *Daphnia magna* is 7.9 μg/L [12].

Adverse effects from exposure to D4 in sediment-dwelling organisms were observed at

concentrations above 44 mg/kg. The experimental toxicity data show that the substance can also

cause long-term toxicity to sensitive pelagic aquatic organisms at relatively low concentrations

(below its water solubility limit of 0.056 mg/L ). Risk quotients derived from exposure scenarios

involving discharges of D4 from both consumer use and industrial operations, show a total of 249

sites (~23.4%) evaluated across Canada have predicted environmental concentrations in water

higher than predicted no-effect concentrations for aquatic organisms. Considering D4’s potential

to bioaccumulate in biota and its high toxicity to sensitive aquatic organisms, long-term

environmental exposure to D4 may cause adverse effects to aquatic organisms in certain

Canadian environments [1].

The lowest NOEC is <0.73 mg/kg dry weight, obtained in a 28-day study with Lumbriculus variegatus (although it should be noted that a higher NOEC of 13 mg/kg dry weight was found for this species in a second study) [12].

Terrestrial compartment

No information for D4 was available for the soil compartment.

1. **Other information**

A search in Scopus yielded 21 peer reviewed articles with focus on health and environment for D4 [8].

Environment Canada concluded that D4 meets the legal definition of toxic. It is also concluded that D4 meets the criteria for persistence as set out in the Persistence and Bioaccumulation Regulations. However, at the time of this screening assessment report, it was not possible to conclude whether D4 meets the criteria for bioaccumulation [1].

The EU PBT Working Group concluded, based on the available information that D4 meets the Annex XIII criteria for both a ‘persistent, bioaccumulative and toxic’ (PBT) and a ‘very persistent and very bioaccumulative’ (vPvB) substance in the environment [13].

1. **References**

[1] Environment Canada Health Canada, Screening Assessment for the Challenge, Octamethylcyclotetrasiloxane (D4), Chemical Abstracts Service Registry Number 556-67-2, November 2008. <https://www.ec.gc.ca/ese-ees/2481B508-1760-4878-9B8A-270EEE8B7DA4/batch2_556-67-2_en.pdf>

[2] Nordic Council of Ministers, Siloxanes in the Nordic Environment, TemaNord 2005:593 ,ISBN 92-893-1268-8, 2005 <http://nordicscreening.org/index.php?module=Pagesetter&type=file&func=get&tid=5&fid=reportfile&pid=4>

[3] Chemspider, [http://www.chemspider.com/ l](http://www.chemspider.com/%20l)

[4] European Commission, Scientific Committee on Consumer Safety (SCCS) , “OPINION ON Cyclomethicone Octamethylcyclotetrasiloxane Cyclotetrasiloxane, D4) and Decamethylcyclopentasiloxane (Cyclopentasiloxane, D5)”, (2010)

[5] Harmonized Classification according to GHS Regulation (EC) No 1272/2008

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[6] International Agency for Research on Cancer (IARC)

<http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[7] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[8] Scopus, primary literature screening search, <http://www.scopus.com/home.url?zone=header&origin=resultslist>

[9] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[10] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[11] Wang, De-Gao, et al. "Review of recent advances in research on the toxicity, detection, occurrence and fate of cyclic volatile methyl siloxanes in the environment." *Chemosphere* Vol. 93, Issue 5, October 2013: 711–725
URL: <http://www.sciencedirect.com/science/article/pii/S0045653512012805>

[12] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

[13] The EU PBT Working Group assessment report on octamethylcyclotetrasiloxane (D4)

# Octamethyl trisiloxane (MDM)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e),***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

1. **Persistence**

Available data indicate both high and low degradation rates in water for MDM. The substance degrades relatively fast in soil depending on the water content. There is no data available for degradation in sediment.

MDM cannot be assessed towards the persistence criteria according to Annex D 1 (b) (i) due to equivocal data.

1. **Bioaccumulation**

Experimental steady state BCF data of 5030 (0.0017 mg/L of MDM) and 7730 (0.021 mg/L) and experimental log Kow of 6.60 are reported for MDM.

MDM is considered to fulfil the bioaccumulation criteria according to Annex D 1 (c) (i).

1. **Long-range transport (LRT)**

MDM present in air will undergo abiotic degradation through reaction with photochemically-produced atmospheric hydroxyl radicals, with atmospheric half-lives of 6–9 days.

MDM is considered to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

Measured effect concentration and NOEC values indicate low ecotoxicity for MDM for aquatic organisms. There were no effect concentration values available for terrestrial organisms.

Therefore MDM is not likely to fulfil the Annex D 1 (e) (i) criteria.

1. **Toxicity to human health**

MDM indicate low oral, dermal and inhalation acute toxicity. MDM is not classified for carcinogenity by IARC. Mutagenicity and reproductive toxicity is negative for MDM.

Therefore MDM is not likely to fulfilthe Annex D 1 (e) (ii) criteria.

**SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [3]

|  |  |
| --- | --- |
| Common name: | Octamethyl trisiloxane (MDM) |
| IUPAC name: | Octamethyltrisiloxane  |
| CAS number: | 107-51-7 |
| Molecular weight: | 236.54 g/mol |
| Chemical structure: | http://images-a.chemnet.com/suppliers/chembase/370/241370.gif |

1. **Chemical group**

Linear volatile methyl siloxanes (linear VMS) [2]

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

|  |  |  |
| --- | --- | --- |
| **Property** | **Value** | **References** |
| Vapour pressure | Experimental: 520Pa(3.9 mm Hg)Estimated: 465 Pa(3.5 mm Hg) | [2] |
| Water solubility | Experimental:0.034 mg/L (at 23°C)Estimated: 0,027 mg/L (at 25°C) | [2] |
| Partition coefficient n-octanol/water (log value) | Experimental:6.60Estimated:6.6 | [2]EpiSuite v.1.68 |
| Partition coefficient air/water (log value) | 2.127 | Epi Suite v 1.10 |
| Partition coefficient air/octanol (log value) | Experimental: 3.72Estimated: 4.5 | [2]Epi Suite v 1.10 |
| Henry’s Law Constant | Experimental: 3.0 × 105 2.9 × 106Estimated:4.23 × 104(0.418 atm·m3/mole; Bond method)4.07 × 106(40.2 atm·m3/mole; VP/Wsol method) 3.62 × 106(35.7 atm·m3/mole; VP/Wsol method) | [2][2][2][2] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS

Regulation (EC) No 1272/2008

No harmonized classification available [4]

1. **Environmental fate properties**

A hydrolysis half-life of 13.7 d (329 h) at pH 7 and 25°C was determined for the substance using an appropriate method. The result is considered reliable [2].

A biodegradation rate in water of 0% in 28 days was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [10].

Soil degradation rates were determined for two different soil types in a reliable study conducted according to generally accepted scientific principles. In air-dried Michigan Londo soil, half-lives (closed tubes) ranged from 1.48 d at 32% RH to 119.5 d at 100% RH at 22.5°C [10].

In air-dried UK loamy silt soil, half-life (closed tubes) was 0.26 d at 32% RH.

In open systems, up to one third of the substance was lost by volatilisation, the amount lost increasing with RH. In open systems volatilisation at 32% RH was not significant, and degradation was rapid at this RH in both open and closed systems, but at 100% RH volatilisation was the predominant removal process (half-life <1d) [10].

1. **Phototransformation/photolysis**

MDM present in air will undergo abiotic degradation through reaction with photochemically-produced atmospheric hydroxyl radicals, with atmospheric half-lives of 6–9 days [1][2].

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

|  |  |  |
| --- | --- | --- |
| **Degradation 50%** | **Days**  | **References** |
| Water | > 18213,7 38 | [2][2]Epi Suite, level III fugacity model |
| Soil  | Exper: 1,48 – 119,5 75 | [10]Epi Suite, level III fugacity model |
| Sediment | 338 | Epi Suite, level III fugacity model |

1. **Potential for long range transport**

MDM present in air will undergo abiotic degradation through reaction with photochemically-produced atmospheric hydroxyl radicals, with atmospheric half-lives of 6–9 days. Modelling predicts that MDM will have significant atmospheric transport potential but is unlikely to be deposited from air into water or soil in remote regions [1][2].

1. **Bioaccumulation**

Steady-state BCF values of 5030 L/kg (1.7 µg/L) and 7730 L/kg (21 µg/L) and kinetic BCF values of 3610 L/kg (1.7 µg/L) and 5600 L/kg (21 µg/L) were determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP [2][10].

Experimental log Kow of 6.60 indicates the potential of MDM to be bioaccumulative [2][10].

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References** |
| 1. Acute toxicity
 |  |
| An LD50 value of >2000 mg/kg (oral) was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. | [10] |
| An LC50 value of >22.6 mg/L for inhalation (analytical) was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. An LD50 value of >2000 mg/kg for dermal toxocity was determined in a reliable study conducted according to an appropriate test protocol, and in compliance with GLP. |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| No cancer classification according to IARC available  | [5] |
| Octamethyltrisiloxane has been tested in a reliable in vitro cytogenetic assay according to OECD TG 473 and under GLP. The test substance did not induce statistically and biologically significant increases in the chromosomal aberration frequency in CHO cells. Appropriate solvent and positive controls were included and gave expected results. It is concluded that the test substance is negative for the induction of chromosome aberrations (is not clastogenic) in vitro under the conditions of the test. | [10] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| In a Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD Guideline 422), performed to GLP, the potential inhalation toxicity of octamethyltrisiloxane was evaluated in Sprague-Dawley rats. Animals were exposed to target concentrations of 0, 800, 1600 or 3200 ppm for 6 hours/day for 29 days in the toxicity test and up to 42 days in the reproductive/developmental screening test. No treatment-related effects were observed in any of the reproductive parameters evaluated. Differences in mean values for the treated groups relative to the control group were small and none were found to be statistically significant. The NOAEC for the reproductive toxicity of octamethyltrisilxoane was 3146 ppm on the basis of this screening test. | [10] |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| Effects on the liver, kidney and lung, as well as reduced body weight gain were observed in rats following repeated-dose exposure to MDM and its analogues. | [2] |
|  |  |
| 1. Mode of action
 |  |
| No data available |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| Due to the moderate to high volatility of MDM and its occurrence in products with “leave-on” applications, inhalation is also considered to be a relevant route of exposure. Comparison of the estimated range of mean-event concentration (0.050– 4.2 mg/m3), from use of cosmetics and personal care products, with the lowest LOAEC following short-term inhalation exposure to MDM (7740 mg/m3), results in margins of exposure ranging from 1840 to 154 800. These margins are considered adequate to address uncertainties in the health effects and exposure databases. | 1. [2][6]
 |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

No observable adverse effects were seen at test concentrations up to the reported water solubility of 0.034 mg/L in acute testing with rainbow trout, *Oncorhynchus mykiss*, the water flea, *Daphnia magna* and the green alga, *Pseudokirchneriella subcapitata*, as well as in chronic testing with *O.* *mykiss* and *D. magna [2].*

No dose-related toxicity was observed in fathead minnow, *Pimephales promelas*, exposed for 42 days to test concentrations of 0.0017 mg/L (0.0034 nominal) and 0.021 mg/L (0.034 nominal) MDM . Although occasional mortalities occurred throughout the study (i.e., 8 to 10 mortalities in each treatment of 120 fish), all surviving fish appeared normal and displayed no overt signs of toxicity [2].

A 28-day toxicity test with the freshwater oligochaete, *Lumbriculus variegates*, and MDM incorporated into a formulated sediment (sediment organic carbon (OC) content 1.9%), found significantly reduced survival and reproduction at a lowest measured test concentration (LOEC) of 1.6 mg/kg sediment dry weight (dw). The lowest no-effect concentration (NOEC) for the study was 1.1 mg/kg dw, based also on endpoints of survival and reproduction. Mean dry weight was not significantly reduced at any test concentration relative to the controls. Survival and reproduction were reported as a single endpoint as specified in toxicity testing guidelines for *Lumbriculus* (e.g., OECD 2007) and were determined as the mean number of living worms present in the test containers at test termination [2].

A 28-day EC50 of >38 mg/kg sediment dry weight has been determined for the effects of the test substance on reproduction and biomass of Lumbriculus variegatus. A NOEC of 38 mg/kg sediment dry weight has also been determined for the same endpoints [10].

A 28-Day LC50 value of 166 mg/kg dry weight has been determined for the effects of the sediment incorporated test substance on mortality of Chironomus riparius. A NOEC of 39 mg/kg dry weight for effects on development rate has been determined in the same test [10].

A 28 day LC50 and NOEC values of >70 and ≥70 mg/kg have been reported for the effects of the test substance on the mortality and growth rate of the freshwater amphipod Hyallela azteca. The results are based on mean measured concentrations [10].

A 28-day EC50 of >17 mg/kg sediment dry weight has been determined for the effects of the test substance on survival and reproduction of Lumbriculus variegatus. A NOEC of 1.1 mg/kg sediment dry weight has also been determined for the same endpoints [10].

Terrestrial compartment

There were no effect concentration data available for terrestrial organisms in the reviewed references.

1. **Other information**

 A search in Scopus yielded 21 peer reviewed articles with focus on health and environment for MDM [7].

No record for MDM was found in the TOXNET HSDB database.

There is no EU PBT assessment report available.

Environment Canada proposed in their screening assessment that MDM is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends or may constitute a danger in Canada to human life or health [12].

1. **References**

[1] Trisiloxane, octamethyl-, (MDM) – Chemical Abstracts Service Registry Number (CAS RN)107-51-7: NGO Response to Draft Screening Assessment & Risk Management Scope Documents in Batch 12 of the Industry Challenge of the Chemicals Management Plan (*Canada Gazette Part I, Vol. 145, No. 2* — January 8, 2011), [http://s.cela.ca/files/780.draft%20RA%20MDM%20(Batch%2012).pdf](http://s.cela.ca/files/780.draft%20RA%20MDM%20%28Batch%2012%29.pdf)

[2] Updated Draft Screening Assessment for the Challenge, Trisiloxane, octamethyl- (MDM) , Chemical Abstracts Service Registry Number 107-51-7, ,March 2014, <https://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=19584F14-1#toc30>

[3] Chemspider, http://www.chemspider.com/

[4] Harmonized Classification according to GHS Regulation (EC) No 1272/2008

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[5] International Agency for Research on Cancer (IARC)

<http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>

[6] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA).

<http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[7] Scopus, primary literature screening search, <http://www.scopus.com/home.url?zone=header&origin=resultslist>

[8] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[9] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[10] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

[11] Nite, Incorporated Administrative Agency, National Institute of Technology and Evaluation <http://www.safe.nite.go.jp/jcheck/SearchAction?request_locale=en>

[12] Environment Canada, Updated Draft Screening Assessment for the Challenge, Octamethyl trisiloxane (MDM) (2014)

# Triisopropylnaftalene (TIPN)

***Overall conclusion: Class 4: Substances that are not likely to meet all Annex D criteria (b), (c), (d) and (e),***

**CONCLUSIONS**

Assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

## Persistence

Degradation of 0-23% in 4 weeks in a screening test for biodegradation in water are reported for TIPN. This suggests a degradation of less than 50% in 2 months.

Triisopropylnaftalene is considered likely to meet the Annex D 1 (b) criteria.

1. **Bioaccumulation**

Experimental data for bioaccumulation with Rice fish (Oryzias latipes) at three different dose levels of the substance namely 1 ppb, 5 ppb and 50 ppb resulted in steady state (10 weeks) BCF values 7600 (1 ppb), 11000 (5 ppb) and 14600 (50 ppb) These BCF values indicate this is a bioaccumulative substance. In Chemspider one experimental BCF is reported namely 138038.

Triisopropylnaftalene is considered to fulfil the Annex D 1 (c) (i) criteria.

1. **Long-range transport (LRT)**

Estimated half-life in air is 0.096 Days [AopWin v1.92].

Triisopropylnaftalene is considered not likely to fulfil the Annex D 1 (d) (iii) criteria.

1. **Ecotoxicity**

No experimental data available in the references reviewed.

Triisopropylnaftalene cannot therefore be assessed towards the Annex D 1 (e) criteria due to insufficient data.

1. **Toxicity to human health**

No experimental data available in the references reviewed.

Triisopropylnaftalene cannot therefore be assessed towards the Annex D 1 (e) criteria due to insufficient data.

 **SUMMARY OF DATA**

1. **Identity of the substance and physical and chemical properties**
2. **Name and other identifiers of the substance**

Table 1: Substance identity [1]

|  |  |
| --- | --- |
| Common name: | Triisopropylnaftalene |
| IUPAC name: | 1,3,5-Triisopropylnaphthalene |
| CAS number: | 35860-37-8 |
| Molecular weight: | 254.42 g/mol |
| Chemical structure: | ChemSpider 2D Image | 1,3,5-Triisopropylnaphthalene | C19H26 |

1. **Chemical group**

Aromatics

1. **Physico-chemical properties**

Table 2: Overview of selected physic-chemical properties

| **Property** | **Value** | **References** |
| --- | --- | --- |
| Vapour pressure | Estimated: 0.00798 Pa (25°C) | Epi Suite v 1.43 |
| Water solubility | Estimated: 0.008181 mg/L (25°C) | Epi Suite v 1.42 |
| Partition coefficient n-octanol/water (log value) | Experimental: BCF: 138038BCF: 7600 - 14600Estimated: log Kow : 7.54 |  [1][10]Epi Suite v 1.68 |
| Partition coefficient air/water (log value) | Estimated: -0.801 | Epi Suite v 1.10 |
| Partition coefficient air/octanol (log value) | Estimated: 8.3 | Epi Suite v 1.10 |
| Henry’s Law Constant | Estimated: 3.87E-003 atm-m3/mole |  [1] |

1. **Classification and labelling**
2. Harmonized Classification according to GHS [6]

Regulation (EC) No 1272/2008

No harmonized classification available

1. **Environmental fate properties**

The Japanese NITE database report degradation of 0-23% in 4 weeks in a screening test for biodegradation in water [9]. This suggests a degradation of less than 50% in 2 months.

1. **Phototransformation/photolysis**

No data available in the references reviewed

1. **Biodegradation**

Table 3: Half-lives in soil, water and sediment

| **Degradation 50%** | **Days**  | **References** |
| --- | --- | --- |
| Water | 38 | Epi Suite, level III fugacity model |
| Soil  | 75 | Epi Suite, level III fugacity model |
| Sediment | 338 | Epi Suite, level III fugacity model |

1. **Potential for long range transport**

Estimated half-life in air is 0.096 Days (AopWin v1.92), so there is likely no estimated potential for LRT.

1. **Bioaccumulation**

Experimental data for bioaccumulation with Rice fish (Oryzias latipes) at three different dose levels of the substance namely 1 ppb, 5 ppb and 50 ppb resulted in steady state (10 weeks) BCF values 7600 (1 ppb), 11000 (5 ppb) and 14600 (50 ppb) [9]. These BCF values indicate this is a bioaccumulative substance.

1. **Human health hazard assessment**

|  |  |
| --- | --- |
| **Health hazard** | **References**  |
| 1. Acute toxicity
 |  |
| No data available |  |
|  |  |
| 1. Mutagenicity and Carcinogenity
 |  |
| No cancer classification according to IARC | [3] |
|  |  |
| 1. Toxicity for reproduction
 |  |
| No data available |  |
|  |  |
| 1. Neurotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Immunotoxicity
 |  |
| No data available |  |
|  |  |
| 1. Endocrine disruption
 |  |
| No data available |  |
|  |  |
| 1. Mode of action
 |  |
| No data available |  |
|  |  |
| 1. Acceptable Exposure levels
 |  |
| No data available |  |

1. **Environmental hazard assessment**

Aquatic compartment (including sediment)

No data available in the references reviewed.

Terrestrial compartment

No data available in the references reviewed.

1. **Other information**

A search in Scopus did not yield any peer reviewed articles with focus on health and environment for triisopropylnaftalene [7]. No record was found in the TOXNET HSDB database [2].

1. **References**

[1] Chemspider, <http://www.chemspider.com/Chemical-Structure.2289772.html?rid=b36604d5-ac14-4692-8b4d-7140fba35f8f>

[2] TOXNET, <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

HSDB/TOXNET database (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>)

[3] International Agency for Research on Cancer (IARC), <http://monographs.iarc.fr/ENG/Classification/ClassificationsCASOrder.pdf>

[4] Institut fur Arbeitsschutz Deutschen Gesetzlichen Unfallversicherung (IFA)., <http://limitvalue.ifa.dguv.de/Webform_gw.aspx>

[5] EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

[6] Harmonized Classification according to GHS Regulation (EC) No 1272/2008,

<http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database>

[7] Scopus, primary literature screening search, http://www.scopus.com/home.url?zone=header&origin=resultslist

[8] ECHA registration data base\*
http://echa.europa.eu/information-on-chemicals

*\*Note: primarily results with reliability level 1 (without restrictions) are referred to and when no level 1 results are available, reliability level 2 (with restrictions) are used.*

[9] Nite, Incorporated Administrative Agency, National Institute of Technology and Evaluation <http://www.safe.nite.go.jp/jcheck/SearchAction?request_locale=en>

[10] Motoharu Suzuki & Chisato Matsumura & Takeshi Nakano & Hiromasa Imaishi, “Investigation of environmental contamination of mono-isopropylnaphthalene, di-isopropylnaphthalene and tri-isopropylnaphthalene in Hyogo in Japan” , Environ Sci Pollut Res, DOI 10.1007/s11356-012-0987-9 (2012), http://ee-net.ne.jp/serbia/paper/suzuki-DIPN.pdf

1. Bench-mark with an isomer with CAS No: 36876-13-8 where HSDB data were available since no environmental fate data of Diisopropyl-1,1'-biphenyl was found since these two isomers have close physical-chemical properties. [↑](#footnote-ref-2)
2. Alternative CAS numbers: 36876-13-8 (TOXNET), and 36919-88-7. [↑](#footnote-ref-3)
3. SRC : Syracuse research center [↑](#footnote-ref-4)
4. Syracuse Research Center model [↑](#footnote-ref-5)
5. **Wemcol** is a technical isopropylbiphenyl formulation [↑](#footnote-ref-6)