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Di-*tert*-dodecyl pentasulfide

MAK Value Documentation – Translation of the German version from 2012

A. Hartwig[1,*] MAK Commission[2,*]

1 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

2 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

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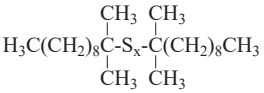
di-*tert*-dodecyl pentasulfide, di-*tert*-dodecyl polysulfide, maximum workplace concentration, MAK value, developmental toxicity, prenatal toxicity, peak limitation

MAK value (2011)	**100 mg/m³ I (inhalable fraction)**
Peak limitation (2011)	**Category II, excursion factor 2**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2011)	**Pregnancy Risk Group C**
Germ cell mutagenicity	–
BAT value	–

Synonyms	no data
Chemical name	di-*tert*-dodecyl pentasulfide di-*tert*-dodecyl polysulfide
CAS number	1) di-*tert*-dodecyl pentasulfide: 31565-23-8 2) di-*tert*-dodecyl polysulfide: 68583-56-2 and 68425-15-0
Structural formula	
Molecular formula	1) $C_{24}H_{50}S_5$ 2) $C_{24}H_{50}S_X$; x = 2–8, mainly 3–5
Molar mass	about 498 g/mol (US EPA 2004)
Melting point	< 0 °C (ECB 2000 a; US EPA 2004)
Boiling point at 1013 hPa	> 200 °C (ECB 2000 a; US EPA 2004)

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Density at 20 °C	1.01 g/cm³ (ECB 2000 a)
Vapour pressure at 20 °C	< 0.03 hPa (ECB 2000 a; US EPA 2004)
log K_{OW}	> 5 (calculated; US EPA 2004)
Solubility	insoluble in water (ECB 2000 a; US EPA 2004)
Stability	di-*tert*-dodecyl polysulfide: stable under normal conditions (Arkema 2009)
Production	no data
Purity	100% (US EPA 2004)
Impurities	none (US EPA 2004)
Uses	sulfidation of catalysts in metal processing and hydrogen treatment; metal processing, iron-free metal processing, steel roller oils, wire-drawing industry; the sulfur reacts with the metal under extreme heat and pressure by forming a metal sulfide layer enhancing sliding capacity and movement, thus reducing friction and damage to metal equipment (US EPA 2004)

The present documentation is based mainly on the summaries published by the US Environmental Protection Agency (US EPA 2004) and the European Chemicals Bureau (ECB 2000 a). The original study reports they quote are not available.

Di-*tert*-dodecyl **poly**sulfide ($C_{24}H_{50}S_X$) consists of isomers with polysulfide chains with a length of x = 2–8, but mainly of 3–5. Most of the studies investigated the di-*tert*-dodecyl **penta**sulfide isomer (x = 5), and these two substances are therefore evaluated together here.

1 Toxic Effects and Mode of Action

Di-*tert*-dodecyl **penta**sulfide is of low toxicity after acute and repeated oral administration. The oral LD_0 in the rat is 12 625 mg/kg body weight, the LD_{50} in the mouse > 20 000 mg/kg body weight, the dermal LD_0 > 2000 mg/kg body weight. Apart from salivation, no substance-related effects occurred in rats at the highest di-*tert*-dodecyl **penta**sulfide dose tested of 1000 mg/kg body weight and day in a 28-day gavage study. Also, neither substance-related effects in the dams nor in the offspring were found in a developmental toxicity study with rats after oral administration on gestation days 6 to 15 up to the highest dose tested of 1000 mg/kg body weight and day.

Di-*tert*-dodecyl **penta**sulfide is, at most, slightly irritating to the skin and eyes of rabbits.

In the maximization test with guinea pigs, di-*tert*-dodecyl **penta**sulfide produced slight non-specific irritation in 4 of 20 animals. These findings may indicate mild skin sensitization.

There are no studies of the carcinogenicity of these compounds. Available in vitro studies with di-*tert*-dodecyl **poly**sulfide and di-*tert*-dodecyl **penta**sulfide provide no evidence of a genotoxic potential.

2 Mechanism of Action

There are no data available.

3 Toxicokinetics and Metabolism

There are no data available.

As there are no reliable data for the solubility in water or the log K_{OW} of the substances, it is not possible to calculate their penetration through the skin.

4 Effects in Humans

There are no data available.

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

There are no data available.

5.1.2 Oral administration

The LD_0 for di-*tert*-dodecyl **penta**sulfide in the rat was 12 625 mg/kg body weight (US EPA 2004). The LD_{50} in the Swiss mouse was greater than 20 000 mg/kg body weight (no other data; ECB 2000 a).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.1.3 Dermal application

In a study carried out according to OECD Test Guideline 402 with di-*tert*-dodecyl **penta**sulfide, the LD_0 in Sprague Dawley rats was greater than 2000 mg/kg body weight. No substance-related effects occurred during the recovery period of 14 days. Neither erythema nor oedema were found, and there were no deaths or behavioural abnormalities (ECB 2000 a; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

There are no data available.

5.2.2 Oral administration

In an 8-day study with administration of di-*tert*-dodecyl **penta**sulfide to rats, mortality was not observed. Increased salivation occurred in all males given 1250 or 2500 mg/kg body weight and day, and in 2 and 3 of 4 females at 1250 and 2500 mg/kg body weight, respectively. Food consumption and body weight gains were slightly reduced in the male animals at 2500 mg/kg body weight. In 3 of 4 female animals in this dose group, the wall of the forestomach was thickened or also transparent. The NOAEL (no observed adverse effect level) was 1250 mg/kg body weight and day based on the reduced body weight gains of the males at 2500 mg/kg body weight and day (US EPA 2004). No data for the number of animals and mode of administration (with the diet or gavage) are available. Presumably, however, 4 male and 4 female animals were treated per dose group.

In a 28-day study according to EEC guidelines, 0, 50, 250 or 1000 mg di-*tert*-dodecyl **penta**sulfide/kg body weight and day was administered to rats by gavage (no other data). No mortality occurred during exposure and the 2-week recovery period. Salivation was increased in all animals of both sexes after the administration of 1000 mg/kg body weight and day, though not during the recovery period. There were no abnormal findings with regard to body weights, food consumption, haematological and clinico-chemical investigations, urinalysis, organ weights, or in the gross and histopathological examinations. The NOAEL was 1000 mg/kg body weight and day (Danish EPA 2005; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

Di-*tert*-dodecyl **penta**sulfide was not irritating to the skin of rabbits in a study carried out according to OECD Test Guideline 404. The substance was applied semi-occlusively to the skin in undiluted form for 4 hours. The mean scores after 24, 48 and 72 hours were 1.72 for erythema and 0.39 for oedema (no other data; ECB 2000 a). The same study was evaluated by the US EPA (2004), and the substance was regarded as slightly irritating. Mild erythema occurred in one animal and moderate erythema in 5 animals, mild oedema was found in 3 animals (no other data; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.3.2 Eyes

In a study according to OECD Test Guideline 405, di-*tert*-dodecyl **penta**sulfide was not irritating to the rabbit eye. The mean scores after 24, 48 and 72 hours were 0.89 and 0.61 for conjunctival swelling and redness, respectively, 0.33 for congestion of the iris and 0.0 for corneal opacity (no other data; ECB 2000 a). The US EPA (2004) evaluated the substance based on the same study as slightly irritating to the rabbit eye due to the observed mild swelling and redness that persisted in 2 animals for 72 hours, and slight congestion of the iris, which lasted up to 48 hours in some of the animals (no other data; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.4 Allergenic effects

In a maximization test with guinea pigs according to OECD Test Guideline 406, di-*tert*-dodecyl **penta**sulfide caused slight irritation in 4 of 20 animals. Intradermal induction was carried out using 1% di-*tert*-dodecyl **penta**sulfide in water, topical induction and the challenge were performed with the undiluted substance. The authors suggested that these reactions could have concealed slight allergic reactions (no other data; Atofina Chemicals Inc 2004 a; ECB 2000 a; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

Also from studies with structurally similar substances, no clearly positive or negative results are available. In a maximization test with 5% di-*tert*-**butyl** polysulfide (CAS No. 68937-96-2), one questionably positive result was obtained; positive reactions occurred only in the first, but not in the repeated challenge (no other data; ECB 2000 b).

However, a well-documented maximization test with di-*tert*-**nonyl** polysulfide (CAS No. 68425-16-1), yielded negative results in 10 male and 10 female guinea pigs after intradermal induction with a 25% solution of the substance in corn oil and epicutaneous induction with a 50% solution in acetone. The challenge was, however, carried out using a low concentration of only 1% di-*tert*-**nonyl** polysulfide in acetone (Atofina Chemicals Inc 2004 b).

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

There are no data available.

5.5.2 Developmental toxicity

In a developmental toxicity study according to OECD Test Guideline 414, di-*tert*-dodecyl **penta**sulfide was administered orally to Sprague Dawley rats on gestation days 6 to 15 at dose levels of 0, 50, 250 or 1000 mg/kg body weight and day, and the foetuses were delivered by caesarean section on day 20 of gestation. Compared with the findings in the controls, there were no treatment-related effects. No clinical toxicity, mortality, abortions or complete resorptions were found. Food consumption and body weight gains, gross-pathological findings and post-implantation losses in the dams were not affected. There was no difference in the number of live offspring per litter, foetal body weights, visceral and skeletal anomalies and variations between the treated rats and controls. The NOAEL was 1000 mg/kg body weight and day for maternal toxicity and prenatal developmental toxicity (Danish EPA 2005; US EPA 2004).

No studies are available for di-*tert*-dodecyl **poly**sulfide.

5.6 Genotoxicity

In a mutagenicity test according to OECD Test Guideline 471 with Salmonella typhimurium TA98, TA100, TA1535, TA1537 and TA1538, di-*tert*-dodecyl **penta**sulfide was not found to be mutagenic in the presence and absence of a metabolic activation system during a 72-hour exposure period (no other data; ECB 2000 a).

A test for chromosomal aberrations with di-*tert*-dodecyl **penta**sulfide in vitro in the presence and absence of a metabolic activation system likewise yielded negative results (no other data; US EPA 2004).

Di-*tert*-dodecyl **poly**sulfide was negative in the $TK^{+/-}$ mutation test with mouse lymphoma cells (no other data; Danish EPA 2005).

As no information on cytotoxicity is provided in any of the available in vitro genotoxicity tests, it is not possible to make any conclusive evaluation of the genotoxicity in vitro.

No in vivo studies of genotoxicity are available.

5.7 Carcinogenicity

There are no data available.

6 Manifesto (MAK value/classification)

Di-*tert*-dodecyl **penta**sulfide is, at most, slightly irritating to the skin and eyes of rabbits. The systemic toxicity of the substance is also low. No target organs can be defined.

MAK value. No studies of repeated inhalation exposure with animals or observations in humans are available from which a MAK value can be derived. Systemic toxicity is low; in a 28-day gavage study with di-*tert*-dodecyl **penta**sulfide in rats, no effects, apart from an increase in salivation, occurred up to the highest dose tested of 1000 mg/kg body weight and day. Due to the low toxicity and the, at most, slight irritation to the skin or eyes, a MAK value is derived based on the subacute (28-day) study. The amount absorbed after ingestion or inhalation is not known and is therefore assumed to be 100%. The following toxicokinetic data are taken into consideration for the extrapolation of the NOAEL to a concentration in workplace air: the species-specific correction value for the rat (1:4), the assumed oral absorption of 100%, the body weight of 70 kg and respiratory volume of 10 m^3 of the

person, and the assumed 100% absorption by inhalation. The concentration calculated from this is 1750 mg/m³. As, however, no chronic studies are available and only one 28-day study, an increase in effects over time cannot be excluded. Therefore, using the preferred value approach, a MAK value of 100 mg/m³ has been established for the inhalable fraction of di-*tert*-dodecyl **penta**sulfide and di-*tert*-dodecyl **poly**sulfide.

Peak limitation. As the MAK value is based on systemic effects, the substances are assigned to Peak Limitation Category II and, due to the absence of data for the half-life, the default excursion factor of 2 has been assigned.

Absorption through the skin. Data for dermal absorption are not available. In the rat, the dermal LD_0 is above 2000 mg/kg body weight. As no reliable data for the solubility of the substances in water and for the log K_{OW} are available, it is not possible to calculate their penetration through the skin. Due to the high molar mass and the probably high log K_{OW}, dermal penetration is presumably low. As the systemic toxicity is also very low, the substances are not designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. No clinical findings for skin or respiratory sensitization are available. A maximization test with the application of di-*tert*-dodecyl **penta**sulfide to the skin of guinea pigs yielded a questionable result, which could at best indicate a low contact sensitization potential. No studies are available for the skin sensitization potential of di-*tert*-dodecyl **poly**sulfide. As experimental animal studies of the skin sensitization potential of structurally related substances yielded negative results, di-*tert*-dodecyl **penta**sulfide and di-*tert*-dodecyl **poly**sulfide are not designated with "Sa" (for substances which cause sensitization of the airways) or "Sh" (for substances which cause sensitization of the skin).

Carcinogenicity and germ cell mutagenicity. No in vivo studies of carcinogenicity or genotoxicity are available. The available in vitro studies provide no evidence of a genotoxic potential. The substances are therefore not classified in one of the categories for carcinogens or germ cell mutagens.

Prenatal toxicity. In a prenatal developmental toxicity study carried out according to OECD Test Guideline 414 in rats, no substance-related effects were found after oral di-*tert*-dodecyl **penta**sulfide doses of up to 1000 mg/kg body weight and day. The following toxicokinetic data are taken into consideration for the extrapolation of the NOAEL to a concentration in the air: the species-specific correction value for the rat (1:4), the assumed oral absorption of 100%, the body weight of 70 kg and respiratory volume of 10 m³ of the person, and the assumed 100% absorption by inhalation. The di-*tert*-dodecyl **penta**sulfide concentration calculated from this is 1750 mg/m³. This concentration is 18 times as high as the MAK value. As no developmental toxicity was induced, and the difference between the NAEC and the MAK value is sufficiently great, the substance is assigned to Pregnancy Risk Group C.

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

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