The MAK Collection for Occupational Health and Safety

Di-tert-dodecyl pentasulfide / Di-tert-dodecyl polysulfide

MAK Value Documentation, addendum – Translation of the German version from 2018

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Di-*tert*-dodecyl pentasulfide, Di-*tert*-dodecyl polysulfide / 2-(2,3,3,4,5,5-Hexamethylhexan-2-ylpentasulfanyl)-2,3,3,4,5,5-hexamethylhexane

MAK value documentation

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Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the maximum concentration at the work place (MAK value), the Pregnancy Risk Group and the absorption through the skin of di-*tert*-dodecyl pentasulfide [31565-23-8] and di-*tert*-dodecyl polysulfide [68583-56-2; 68425-15-0].

The systemic toxicity is low and the substances are at most minimally irritating to skin and eye. Acidophilic globuli are present in the kidney of male rats in an oral 28-day study at 50 mg/kg body weight and day, presumably resulting from an α2u-globulin mediated kidney toxicity which, however, has not actually been proven. Based on this LOAEC the MAK value would be 10 mg/m^3. However, the substances are poorly water-soluble liquids and an accumulation in the lung is expected. Most of the di-*tert*-dodecyl pentasulfide and di-*tert*-dodecyl polysulfide molecule consists of hydrocarbon chains resulting in characteristics similar to severely refined mineral oil, for which a MAK value of 5 mg/m^3 had been set as the respirable fraction (R) based on inhalation studies. Therefore, the MAK-value for di-*tert*-dodecyl pentasulfide and di-*tert*-dodecyl polysulfide is also set at 5 mg/m^3 R. Peak Limitation is designated as well by analogy with severely refined mineral oil with Category II and excursion factor of 4.

New data on developmental toxicity are not available. As the MAK value is lowered, Pregnancy Risk Group C is retained. Skin contact is not expected to contribute significantly to systemic toxicity.

Keywords

di-*tert*-dodecyl pentasulfide; di-*tert*-dodecyl polysulfide; 2-(2,3,3,4,5,5-hexamethylhexan-2-ylpentasulfanyl)-2,3,3,4,5,5-hexamethylhexane; peak limitation; prenatal toxicity; absorption through the skin; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

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Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide

[31565-23-8; 68425-15-0; 68583-56-2]

Supplement 2018

MAK value (2017)	**5 mg/m³ R (respirable fraction)**
Peak limitation (2017)	**Category II, excursion factor 4**
Absorption through the skin	**–**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2011)	**Pregnancy Risk Group C**
Germ cell mutagenicity	**–**
BAT value	**–**

Molar mass	about 498 g/mol (US EPA 2004)
Melting point	–48 to +28 °C (ECHA 2017 a)
Boiling point at 1013 hPa	193.7–238.5 °C (ECHA 2017 a)
Density at 20 °C	1.0028 g/cm³ (ECHA 2017 a)
Vapour pressure at 20 °C	4.17×10^{-6} hPa (ECHA 2017 a)
log K_{OW} [1)]	> 12 (calculated; ECHA 2017 a)
Solubility	0.26 µg/l water (ECHA 2017 a)

In the ECHA databank a registration dossier is available for di-*tert*-dodecyl polysulfide (ECHA 2017 a). A DNEL of 32.9 mg/m³ was derived. Because of the suspected accumulation of the substance in the lungs resulting from its poor solubility in water, the MAK value has been re-evaluated.

Di-*tert*-dodecyl polysulfide is a mixture of branched C11 to C13 hydrocarbons at the ends of a chain of 2 to 6 sulfur atoms. The mixture is used as an additive in lubricants, greases and metal-working fluids (ECHA 2017 a). The former name di-*tert*-dodecyl **penta**sulfide for di-*tert*-dodecyl polysulfide is no longer used.

1) octanol/water partition coefficient

The original report of the 28-day study described in the documentation from 2012 (documentation "Di-*tert*-dodecyl pentasulfide/Di-*tert*-dodecyl polysulfide" 2012) which was carried out in Sprague Dawley rats according to OECD Test Guideline 407 with daily di-*tert*-dodecyl polysulfide doses of 0, 50, 250 or 1000 mg/kg body weight and day, is now available (Elf Aquitaine Production 1996).

In the male animals of the 28-day study, acidophilic globuli were found in the epithelia of the kidneys at the lowest dose tested and above. This indicates that the substance can be absorbed orally. At the highest dose tested of 1000 mg/kg body weight and day salivation was observed. Histopathological observations in the kidneys of male animals included minimal to moderate acidophilic globuli in the epithelium of the cortical tubuli in 3/6 and 5/6 animals, respectively, at 50 and 250 mg/kg body weight and day, and minimal to slight acidophilic globuli in all the treated male animals at 1000 mg/kg body weight and day. This finding was not observed in the control animals and was not completely reversible in the high dose group up to the end of the recovery period. The authors attribute this finding to the accumulation of α2u-globulin and therefore regard it as species-specific and not relevant to the evaluation. Some male animals were found to have an enlarged renal pelvis at 250 and 1000 mg/kg body weight and day, and in one male and one female animal of the high dose group mineralization of the kidneys was observed (Elf Aquitaine Production 1996). The accumulation of α2u-globulin in male rats has meanwhile been proven for di-*tert*-dodecyl **di**sulfide which is contained in di-*tert*-dodecyl polysulfide (ECHA 2017 b); the findings in the kidneys of male rats after exposure to di-*tert*-dodecyl polysulfide can therefore very probably be attributed to the accumulation of α2u-globulin and are thus not relevant for humans. In addition, α2u-globulin accumulation in the kidneys of male rats is known for linear and branched hydrocarbons from C10 to C15 (Alden 1986).

There were also a number of findings in the high dose group given 1000 mg/kg body weight and day which were not yet statistically significant but show that this dose is close to the LOAEL (lowest observed adverse effect level) for the female animals. In the high dose group the erythrocyte count, haemoglobin concentration and haematocrit value were slightly increased in both sexes (5%–7%). The reductions in the absolute and relative thymus weights were not statistically significant in either sex (absolute: –2%, –8%, –15% in the male animals and –8%, –4%, –13% in the female animals at 50, 250 and 1000 mg/kg body weight and day; relative: –1%, –4%, –9% in the male animals and –1%, +3%, –7% in the female animals). The increase in the absolute (12%) and relative (29%) thyroid weights of the female animals of the high dose group was not statistically significant. As only very few values were outside the normal range of scatter, and the changes were not significant or accompanied by histopathological findings, these effects were not regarded as adverse and the NOAEL (no observed adverse effect level) was established at 1000 mg/kg body weight and day (Elf Aquitaine Production 1996).

At the end of the recovery period the absolute (8%) and relative (8%, statistically significant) kidney weights were increased in the female animals of the high dose group. In both sexes of the high dose group, the increases in the absolute weights (13% and 18%, respectively, in the male and female animals) and the relative weights (22% and 19%, respectively, in the male and female animals) of the mesenteric lymph nodes were not statistically significant. A statistically significant reduction (21%) in the

absolute and relative weights of the mandibular lymph nodes of the female animals of the high dose group was found, as well as an increase in the absolute (19%) and relative (17%) spleen weights that was not significant. As only very few values were outside the normal range of scatter, and most of the changes were not significant or accompanied by histopathological findings and did not occur at the end of the treatment, these effects were not regarded as adverse (Elf Aquitaine Production 1996).

Di-*tert*-dodecyl polysulfide was not found to be irritating to the skin of rabbits in a study carried out according to OECD Test Guideline 404. The undiluted substance was applied semi-occlusively to the skin for 4 hours. The means of the 24-hour, 48-hour and 72-hour scores were 1.72 for erythema and 0.39 for oedema (no other details). On the basis of the same study, the US EPA (2004) assessed the substance as causing slight irritation (no other details) (documentation "Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide" 2012).

Di-*tert*-dodecyl polysulfide was not found to be irritating to the rabbit eye in a study carried out according to OECD Test Guideline 405. The mean values after 24, 48 and 72 hours were 0.89 and 0.61, respectively, for swelling and reddening of the conjunctiva, 0.33 for congestion of the iris, and 0.0 for corneal opacity (no other details). On the basis of the same study, the US EPA (2004) assessed the substance as causing slight irritation in the rabbit eye because of the mild swelling and reddening, which persisted in 2 animals for 72 hours, and the slight congestion of the iris, which in some animals persisted for up to 48 hours (no other details) (documentation "Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide" 2012).

The data do not fulfil the criteria for skin or eye irritants according to the globally harmonized system of classification and designation (ECHA 2017 a).

Manifesto (MAK value/classification)

Di-*tert*-dodecyl polysulfide is, at the most, slightly irritating to the skin and eyes in rabbits. The substance is also systemically hardly toxic. There are no apparent target organs (documentation "Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide" 2012). The mixture is used also in metal-working fluids, where aerosol formation cannot be excluded. As a result of the poor solubility in water of di-*tert*-dodecyl polysulfide, after exposure to aerosol material, accumulation, and therefore effects in the lungs are to be expected.

MAK value. In view of the low toxicity and, at the most, minimal irritation of the skin and eyes, in 2011 a MAK value of 100 mg/m³ I (inhalable fraction) was derived on the basis of the 28-day study with the NOAEL of 1000 mg/kg body weight (documentation "Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide" 2012). In the meantime, the original report of the oral 28-day study has become available (Elf Aquitaine Production 1996). The NOAEL of 1000 mg/kg body weight and day has been confirmed.

The amount absorbed orally and by inhalation is unknown 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 of 1:4, the assumed oral absorption of 100%, the

body weight (70 kg), respiratory volume (10 m^3) and the assumed 100% absorption by inhalation of the person, a possible increase in the effects with chronic exposure (1:6) and the daily exposure of the animals in comparison with the 5 days per week at the workplace (7:5). The concentration calculated from this is 408 mg/m^3. After extrapolation of the data from the animal study to humans (1:2) and application of the Preferred Value Approach, a MAK value of 200 mg/m^3 would be obtained for the inhalable fraction.

However, the substance is poorly soluble in water, and accumulation in the lungs is therefore possible. There are no data available for the metabolism of the substance. For insoluble solids, the General Threshold Limit Value for Dust applies (supplement "General threshold limit value for dust (R fraction) (Biopersistent granular dusts)" 2012), di-*tert*-dodecyl polysulfide, however, is a poorly soluble liquid. As an organic molecule, di-*tert*-dodecyl polysulfide is presumably degraded by the macrophages, so that it probably accumulates to a lesser extent than biopersistent granular dusts. The molecule consists mainly of long hydrocarbon chains. Therefore the properties of the substance are similar to those of severely refined mineral oil, which likewise is a poorly soluble liquid (< 0.1 mg/l water depending on the number of carbon atoms (documentation "Mineral oils (petroleum), severely refined" 2018)) made up of long-chain hydrocarbons. Unlike di-*tert*-dodecyl polysulfide, which is not bacterially biodegradable in 28 days (ECHA 2017 a), severely refined mineral oil is, however, inherently biodegradable, in 28 days by up to 31% (ECHA 2017 c). It is not known whether this difference applies also for degradation via macrophages. The solubility of the substance in the lung fluid may differ from its solubility in water. As its solubility in lung fluid is not known, its solubility in water is used as a surrogate. A MAK value of 5 mg/m^3 R (respirable fraction) was derived for severely refined mineral oil from inhalation studies. By analogy with severely refined mineral oil, a MAK value of 5 mg/m^3 R has therefore been established for di-*tert*-dodecyl polysulfide.

Peak limitation. Peak limitation has also been set in analogy to severely refined mineral oil, so that the substance is classified in Category II with an excursion factor of 4.

Prenatal toxicity. New data for prenatal toxicity have not been published since the documentation from 2012 (documentation "Di-*tert*-dodecyl pentasulfide / Di-*tert*-dodecyl polysulfide" 2012). As the MAK value has been lowered, Pregnancy Risk Group C has been retained.

Absorption through the skin. There are no studies available of the absorption of the substance through the skin. The log K_{OW} is greater than 12 and therefore outside the valid range for the mathematical models for calculating skin penetration. In view of the high molar mass, relevant absorption via the skin is unlikely. In addition, the systemic toxicity is low. The substance is therefore not designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

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