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2,2′-Thiobis(4-methyl-6-*tert*-butylphenol)

MAK Value Documentation – Translation of the German version from 2022

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Keywords

2,2′-thiobis(4-methyl-6-tert-butylphenol); thyroid; general limit value for dust, inhalable fraction; genotoxicity; carcinogenicity; reproductive toxicity; maximum workplace concentration; MAK value; peak limitation

Abstract

The German Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) summarized and evaluated the data for 2,2′-thiobis(4-methyl-6-tert-butylphenol) [90-66-4] to derive an occupational exposure limit value (maximum concentration at the workplace, MAK value), considering all toxicological end points. 2,2′-Thiobis(4-methyl-6-tert-butylphenol) is neither irritating to the human skin in vitro nor irritating to the eyes of rabbits. In a gavage study carried out according to OECD Test Guideline 422, the incidence and severity (minimal to slight) of follicular hypertrophy in the thyroid glands of male rats were increased at 150 mg/kg body weight and day and above. Additionally, slight changes in the colloid were observed at 500 mg/kg body weight and day. The Commission determined a NOAEL of 50 mg/kg body weight and day for this study. This dose has been scaled to a concentration of 10 mg/m^3 I (inhalable fraction), a level of exposure protective against systemic effects. As 2,2′-thiobis(4-methyl-6-tert-butylphenol) is used diluted in metal-working fluids, the technically based limit value of 10 mg/m^3 prevents toxicity if the dissolved solid is inhaled during this application. To prevent the induction of unspecific effects in the respiratory tract by the poorly soluble substance (< 8 µg/l water), the MAK value has been set at the level of the general dust limit value of 4 mg/m^3 I. Peak limitation is regulated in accordance with Section V f) and g) of the List of MAK and BAT Values. A study with the substance was carried out according to OECD Test Guideline 422. As this study does not include a complete investigation of teratogenicity, 2,2′-thiobis(4-methyl-6-tert-butylphenol) has been assigned to Pregnancy Risk Group D. The substance is not genotoxic in vitro and there are no in vivo data. No carcinogenicity study has been performed. Skin contact is expected to make a relatively minor contribution to systemic toxicity. The available data show no evidence of sensitization.

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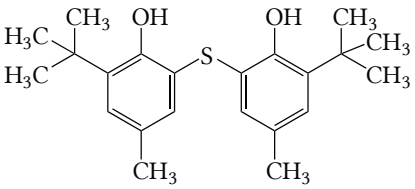
MAK value (2021)	**4 mg/m³ I (inhalable fraction)**
Peak limitation (2021)	**see Section V f) and g) of the List of MAK and BAT Values**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2021)	**Pregnancy Risk Group D**
Germ cell mutagenicity	–
BAT value	–
Synonyms	bis(5-methyl-3-tert-butyl-2-hydroxyphenyl) monosulfide 6,6′-di-tert-butyl-2,2′-thiodi-p-cresol 2,2′-dihydroxy-3,3′-di-tert-butyl-5,5′-dimethyldiphenyl sulfide 2,2′-thiobis(6-tert-butyl-p-cresol) 2,2′-thiobis(6-(1,1-dimethylethyl)-4-methylphenol
Chemical name (IUPAC)	2-tert-butyl-6-(3-tert-butyl-2-hydroxy-5-methylphenyl)-sulfanyl-4-methylphenol
CAS number	90-66-4
Structural formula	
Molecular formula	$C_{22}H_{30}O_2S$
Molar mass	358.5 g/mol
Melting point	82.7–83.9 °C (ECHA 2019)
Boiling point at 970 hPa	305 °C (ECHA 2019)
Density at 20 °C	1.135 g/cm³ (ECHA 2019)
Vapour pressure at 20 °C	0.00000609 hPa (ECHA 2019)
log K_{OW}	> 6.5 at 25 °C (ECHA 2019)
Solubility	< 8 µg/l water at 20 °C (ECHA 2019)
Hydrolytic stability	no data
Stability	no data
Production	no data
Purity	99.8% (ECHA 2019)
Impurities	no data
Uses	antioxidant and heat stabilizer (Special Chem 2020)
Ban on use	no data
Concentrations used	in hydraulic fluids and lubricants: 0.2%; in metal-working fluids: no data (Hartwig and MAK Commission 2018, available in German only)

The documentation is based primarily on the registration data publicly available under REACH (ECHA 2019). Cited unpublished toxicological studies from companies have been made available to the Commission.

1 Toxic Effects and Mode of Action

The physicochemical properties of 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) suggest that it is not well absorbed either by inhalation, oral administration or via the dermal route.

A combined study of the toxic effects of repeated oral doses and a screening test for reproductive and developmental toxicity according to OECD Test Guideline 422 revealed effects only in male rats. In the thyroid gland, the incidences and severity (minimal to slight) of follicular hypertrophy were increased at doses of 150 mg/kg body weight and day and above and changes in the colloid (minimal to slight) were observed at 500 mg/kg body weight and day. Effects on fertility or perinatal toxicity were not detected up to the high dose.

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not found to be genotoxic in a mutagenicity test in various Salmonella typhimurium strains, in a $TK^{+/-}$ mutation test with L5178Y mouse lymphoma cells and in a chromosomal aberration test in V79 cells; all 3 tests were carried out according to the relevant OECD test guidelines. Studies of genotoxicity in vivo or of carcinogenicity are not available.

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) does not cause irritation of the human skin in vitro or irritation of the eyes in rabbits. Clinical findings of contact sensitization caused by 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) are not available. No sensitizing potential was detected in a local lymph node assay up to a concentration of 50%.

2 Mechanism of Action

Mechanistic data for the effects on the thyroid gland are not available.

As the substance is poorly soluble in water, it is assumed that any fraction of the powdery substance in the respirable range would accumulate in the lungs. If the particles accumulate to the point of overloading, this may lead to carcinogenic effects on the lungs. However, the data available for the aerodynamic diameter of a commercial product indicate that the substance does not occur in respirable form (ECHA 2019). It is not known whether the substance is used for products with different aerodynamic diameters.

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

There are no studies available.

Its very low vapour pressure (6.09×10^{-6} hPa at 20 °C) and high boiling point (≥ 305 °C) do not suggest respiratory exposure to the vaporous substance. The data for a powdery commercial product show that it does not reach the thorax because of its large aerodynamic diameter (90% < 480 µm; 50% < 184 µm; 10% < 47 µm) (ECHA 2019). It is unclear whether the substance is or can be produced in respirable diameters.

A study with repeated oral doses of the substance dissolved in propylene glycol given to rats (see Section 5.2.2) reported effects on the thyroid gland at 150 mg/kg body weight and day. This suggests that dissolved 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) is absorbed after oral administration, however, the amount taken up is not known.

There are no experimental data available for absorption through the skin. In addition, models (Fiserova-Bergerova et al. 1990; Tibaldi et al. 2014) cannot be used to estimate the level of absorption through the skin because the log K_{OW} of the substance was > 6 in a study carried out according to OECD Test Guideline 117 (ECHA 2019) and is thus outside the range of validity of the models. However, because of its poor solubility in water, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) is not assumed to be absorbed through the skin in relevant amounts.

3.2 Metabolism

There are no data available.

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

In a study of acute toxicity from 2017 that was carried out according to OECD Test Guideline 423, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not lethal in 6 female Wistar rats at a dose of 2000 mg/kg body weight. There were no treatment-related clinical signs or gross-pathological findings. Likewise, no changes in body weights were found during the observation period of 14 days (ECHA 2019).

5.1.3 Dermal application

In 2017, a limit test with 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was carried out in 5 male and 5 female Wistar rats according to OECD Test Guideline 402. After the test material was mixed to a paste and applied semi-occlusively for 24 hours, it was not found to be lethal at 2000 mg/kg body weight. There were no treatment-related clinical signs or gross-pathological findings. Likewise, no changes in body weights were found during the observation period of 14 days. Local irritation was not observed (ECHA 2019).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

There are no data available.

5.2.2 Oral administration

In a combined study of the toxic effects of repeated oral doses and a screening test for reproductive and developmental toxicity according to OECD Test Guideline 422, groups of 10 male and 10 female Wistar rats were given daily gavage

doses of 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%). The doses were 0, 50, 150 or 500 mg/kg body weight and day; the test substance was dissolved in propylene glycol. In a range-finding study, all 3 females had ruffled fur (males were not tested) at the highest dose of 500 mg/kg body weight; the body weight gains stagnated in 2 animals and were decreased by 4% in 1 animal. In addition, feed consumption was reduced. In the main study, the males and females were first exposed for 14 days; this was followed by a mating period lasting another 14 days, during which the animals continued to be exposed. The males were exposed for 31 days, the females up to postnatal day 13 of the offspring, which corresponded to 50 to 56 days of exposure. No animals died and treatment-related clinical signs were not observed. Feed consumption, body weights or body weight gains were not affected by the treatment. No substance-induced effects on haematology, clinical chemistry or serum T4 levels were found. Likewise, the neurological examinations did not reveal treatment-related effects. The organ weights of the treated animals did not differ from those of the control animals. The gross-pathological examination did not yield any unusual findings. The findings obtained in the thyroid glands of the males are shown in Table 1: The incidences and severity (minimal to slight) of follicular hypertrophy were increased at doses of 150 mg/kg body weight and day and above, and minimal to slight changes in the colloid were observed at 500 mg/kg body weight and day (Charles River Laboratories Den Bosch B.V. 2017).

Tab. 1 Findings in the thyroid glands of male rats given oral doses of 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (Charles River Laboratories Den Bosch B.V. 2017)

	Dose (mg/kg body weight)			
	0	**50**	**150**	**500**
number of animals examined	5	5	5	5
follicular hypertrophy				
minimal	1	1	3	1
slight	0	0	1	4
changes in the colloid				
minimal	0	0	0	1
slight	0	0	0	3

The authors established a parental NOAEL (no observed adverse effect level) of 150 mg/kg body weight and day on the basis of the histopathological findings in the thyroid glands of the males at 500 mg/kg body weight and day (Charles River Laboratories Den Bosch B.V. 2017). In many cases, at this grade of severity, the hypertrophy observed in the thyroid gland is initially adaptive and reversible. Hypertrophy of the thyroid gland may be a precursor of thyroid hyperplasia. Epidemiological studies have demonstrated that the prolonged persistence of thyroid hyperplasia increases the risk of developing thyroid carcinomas. A relevance for humans cannot be excluded. Although, when considered alone, the effects observed at 150 mg/kg body weight and day were not adverse, this was the dose at which the dose–response curve of the effects on the thyroid gland started. The Commission therefore regards the dose of 50 mg/kg body weight and day as the NOEL (no observed effect level).

5.2.3 Dermal application

There are no data available.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

A limit test carried out according to OECD Test Guideline 402 in 2017 was described in Section 5.1.3. The 24-hour semi-occlusive treatment of 5 male and 5 female Wistar rats with 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) mixed to a paste did not cause local irritation of the shaved dorsal skin (ECHA 2019).

An in vitro test with reconstructed human epidermis carried out according to OECD Test Guideline 431 investigated 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) for its potential to induce corrosive effects. In the EpiSkin^{TM}(SM) test system, the irritant or corrosive potential of a substance is determined based on its cytotoxicity in the MTT test (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test). If the relative cell viability is below 35% of that of the negative control after incubation for 4 hours, the substance is regarded as corrosive. The treatment of the cells with 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) led to a cell viability that was 87.4% of that of the negative control. Therefore, the substance was regarded as non-corrosive. The concurrent positive control verified the functioning of the test system (ECHA 2019).

In another in vitro test with reconstructed human epidermis in the EpiSkin^{TM}(SM) test system, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) was investigated for its irritant potential according to OECD Test Guideline 439. The skin was exposed to the test substance for 15 minutes, then washed and incubated without test substance for another 42 hours. In the MTT test, a substance with a relative cell viability 50% below that of the negative control is considered an irritant. After treatment with 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%), the cells were found to have a viability of 76.5% compared with the values of the negative control. Therefore, the substance was considered not to cause skin irritation. The concurrent positive control verified the functioning of the test system (ECHA 2019).

5.3.2 Eyes

In a study of eye irritation carried out in 3 New Zealand White rabbits according to OECD Test Guideline 405, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not found to cause irritation. The eyes were rinsed 1 hour after the instillation of 0.1 g of the test substance into the rabbit eye because the solid substance was still present in the eye. At this time, mild redness of the conjunctivae, conjunctival swelling and lacrimation were observed. These effects were no longer detected after 24, 48 and 72 hours (ECHA 2019).

In an in vitro test carried out in isolated chicken eyes according to OECD Test Guideline 438, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) was investigated for its potential to cause eye irritation. 2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was applied to the eye in an amount of 30 mg and rinsed off after 10 seconds. The test substance did not cause irritation. The concurrent positive and negative controls verified the functioning of the test system (ECHA 2019).

5.4 Allergenic effects

5.4.1 Sensitizing effects on the skin

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was examined in a local lymph node assay carried out with female CBA/Ca mice according to OECD Test Guideline 429. The test substance was dissolved in acetone/olive oil (4:1 v/v) in 3 concentrations between 10% and 50% (maximum solubility), yielding stimulation indices of 1.1, 1.1 and 1.2 (ECHA 2019). Therefore, the results are regarded as negative.

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) was examined in the direct peptide reactivity assay according to OECD Test Guideline 442C. The test results did not yield evidence of reactivity (ECHA 2019). However, the negative test results are uncertain because not all validity criteria were met (precipitate formation).

Furthermore, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was tested in vitro by KeratinoSens assay according to OECD Test Guideline 442DA. The results of the test were negative (ECHA 2019). However, the negative results are uncertain because it was not possible to produce a stable dispersion even with a concentration of 250 µM. A validity criterion required by the protocol of the OECD Test Guideline is a stable dispersion up to a concentration of < 1000 µM.

5.4.2 Sensitizing effects on the airways

There are no data available.

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

The combined study of reproductive and developmental toxicity according to OECD Test Guideline 422 that was described in Section 5.2.2 did not reveal any adverse effects in the female rats up to the high dose of 500 mg/kg body weight and day. In the males, marginal follicular hypertrophy of the thyroid gland was observed at doses of 150 mg/kg body weight and day and above. These findings were minimal to slight at 500 mg/kg body weight and day. Furthermore, changes in the colloid were found at 500 mg/kg body weight and day. Substance-induced effects on the reproductive parameters were not detected up to the high dose. The examined parameters included mating, fertility and conception indices, time until mating, number of implantations, oestrus cycle, sperm profile and the histopathological examination of the reproductive organs. Likewise, the gestation index was not affected by exposure to the substance. Therefore, the NOAEL for effects on fertility was the high dose tested of 500 mg/kg body weight and day (Charles River Laboratories Den Bosch B.V. 2017; ECHA 2019).

5.5.2 Developmental toxicity

Developmental toxicity studies are not available.

The study described above that was carried out according to OECD Test Guideline 422 did not reveal any effects on the duration of gestation, parturition, the sex ratio of the offspring, early postnatal development, the body weights of the offspring, the anogenital distance, areola retention or T4 thyroid levels up the highest dose tested of 500 mg/kg body weight and day; likewise, no findings were obtained in the gross-pathological examination of the thyroid glands of the offspring (Charles River Laboratories Den Bosch B.V. 2017; ECHA 2019). Therefore, the NOAEL for perinatal toxicity is 500 mg/kg body weight and day.

Studies that follow the protocol of OECD Test Guideline 422 include only external, but no skeletal or visceral examinations of the offspring. For this reason, the examination of teratogenicity is not fully covered.

5.6 Genotoxicity

5.6.1 In vitro

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not genotoxic in a mutagenicity test carried out according to OECD Test Guideline 471 with the Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 and with Escherichia coli WP2 uvrA in the presence or absence of a metabolic activation system. Concentrations up to 5000 µg/plate were tested and did not lead to cytotoxicity but to the formation of precipitates at the highest concentration (ECHA 2019).

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not clastogenic in the chromosomal aberration test carried out according to OECD Test Guideline 473 in the presence or absence of a metabolic activation system. In the first assay, V79 cells of Chinese hamsters were exposed for 3 hours to concentrations up to 250 µg/ml without the addition of a metabolic activation system and up to 500 µg/ml with the addition of a metabolic activation system, followed by the analysis of the cells 20 hours later. Precipitates formed at concentrations of 83.33 µg/ml and above without the addition of a metabolic activation system and at 166.67 µg/ml and above in the presence of a metabolic activation system; marked cytotoxicity was observed at concentrations of 27.78 µg/ml and above (63%). A second assay was discarded because a procedural error was made and an insufficient number of cells were plated. Therefore, a third assay was carried out.

The V79 cells were exposed for 3 hours to concentrations up to 10 µg/ml without the addition of a metabolic activation system and up to 500 µg/ml in the presence of a metabolic activation system; this was followed by the analysis of the cells 20 hours later. As in the first assay, precipitates formed and marked cytotoxicity was observed at 6 µg/ml and above (65%) in the system without metabolic activation. The number of cells with chromosomal aberrations was not increased with statistical significance in any of the assays (ECHA 2019).

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) dissolved in acetone was not found to be genotoxic in a $TK^{+/-}$ mutation assay with L5178Y mouse lymphoma cells carried out according to OECD Test Guideline 490. The substance was tested up to cytotoxicity or the solubility limit. The cells were exposed for 3 hours to concentrations up to 2000 µg/ml in the presence and absence of a metabolic activation system. In another assay, the cells were exposed for 24 hours to concentrations up to 70 µg/ml without the addition of a metabolic activation system. Nearly all of the positive findings were obtained at severely cytotoxic concentrations with a relative total growth (RTG) of < 10%. The mutation frequency was increased only in 1 of 2 assays and only at 62.5 µg/ml with an RTG of 18% after incubation for 3 hours without the addition of a metabolic activation system. Although the increase was statistically significant, it did not exceed the level for a biologically relevant increase in mutation frequencies. No evidence of an increase in mutation frequency was found in a second assay carried out under the same conditions. Overall, the results of the test were therefore regarded as negative (ECHA 2019).

5.6.2 In vivo

There are no data available.

5.7 Carcinogenicity

There are no data available.

6 Manifesto (MAK value/classification)

Follicular hypertrophy and slight changes in the colloid of the thyroid gland in male rats are the critical effects after repeated oral administration. There are no data available for effects in humans.

MAK value. 2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) does not cause irritation of the human skin in vitro or irritation of the eyes in rabbits.

A combined study of the toxic effects of repeated oral doses and a screening test for reproductive and developmental toxicity according to OECD Test Guideline 422 revealed increased incidences and severity (minimal to slight) of follicular hypertrophy in the thyroid gland of male rats at 150 mg/kg body weight and day and above and slight changes in the colloid at 500 mg/kg body weight and day. Therefore, the dose of 50 mg/kg body weight and day has been established by the Commission as the NOEL for this study (see Section 5.2.2).

There are no quantitative data available for oral absorption. The following toxicokinetic data are used to extrapolate the NOEL of 50 mg/kg body weight and day to a concentration in workplace air: the daily exposure of the animals in comparison with exposure for 5 days a week at the workplace (7:5), the corresponding species-specific toxicokinetic correction value for the rat (1:4), the body weight (70 kg) and the respiratory volume (10 m^3) of the person. Oral absorption and absorption by inhalation have not been included in the calculation because of the poor solubility of the substance, which leads to the removal of the inhalable fraction that is deposited in the upper respiratory tract by swallowing. For this reason, the amount taken up after inhalation exposure is equivalent to that absorbed after oral exposure. The concentration calculated is thus 122.5 mg/m^3. Taking into consideration that this value was derived from a NOEL from animal studies (1:2) and that the effects may increase with time (1:6), a concentration of 10.2 mg/m^3 is obtained. By applying the preferred value approach, a MAK value of 10 mg/m^3 has been derived for the inhalable fraction.

2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) is a solid. Its solubility in water is < 8 µg/l at 20 °C. The general threshold limit value for dust of 4 mg/m³ for the inhalable fraction (Greim 1999) has been chosen as the MAK value for 2,2′-thiobis-(4-methyl-6-*tert*-butylphenol) to ensure that the value is set at a level that also protects against the non-specific effects induced by the poorly soluble substance on the respiratory tract. As the MAK value would be 10 mg/m³ if it were derived from the findings in rats given oral doses of the dissolved substance, this value also provides protection against possible systemic effects.

The substance is present in metal-working fluids in dissolved form, which may lead to the formation of aerosols. As the technically based limit value for metal-working fluids of 10 mg/m³ must be observed and, additionally, the substance is present in diluted form, systemic toxicity is not expected to occur from dissolved substance taken up from metal-working fluids.

Peak limitation. 2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) has been classified according to Section V f) and g) of the List of MAK and BAT Values.

Prenatal toxicity. Developmental toxicity studies are not available.

A study carried out according to OECD Test Guideline 422 with gavage doses given to Wistar Han rats did not report substance-induced effects on the offspring or the pregnancy parameters up to the highest dose tested of 500 mg/kg body weight and day. As a result, this dose has been established as the NOAEL for perinatal toxicity (Charles River Laboratories Den Bosch B.V. 2017; ECHA 2019).

As the study was carried out according to OECD Test Guideline 422, it did not include a complete examination of teratogenicity. Therefore, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) has been classified in Pregnancy Risk Group D.

Carcinogenicity and germ cell mutagenicity. 2,2′-Thiobis(4-methyl-6-*tert*-butylphenol) (purity: 99.8%) was not genotoxic in a mutagenicity test in various Salmonella typhimurium strains, a $TK^{+/-}$ mutation test with L5178Y mouse lymphoma cells or a chromosomal aberration test in V79 cells; all 3 tests were carried out according to the relevant OECD test guidelines. Studies of genotoxicity in vivo or of carcinogenicity are not available. Based on the present data, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) has not been classified as a carcinogen or in any of the germ cell mutagen categories.

Absorption through the skin. Experimental studies for absorption through the skin are not available. The dermal LD_{50} is higher than 2000 mg/kg body weight. The models cannot be used to estimate the level of absorption through the skin because the log K_{OW} is > 6. However, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) is not expected to be absorbed through the skin in systemically relevant amounts because of its poor solubility in water. The substance has therefore not been designated with an “H” (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. Clinical findings of contact sensitization caused by 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) are not available. A sensitizing potential was not detected in a local lymph node assay up to a concentration of 50%. Therefore, 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) has not been designated with “Sh” (for substances which cause sensitization of the skin). No findings are available for the sensitizing effects of 2,2′-thiobis(4-methyl-6-*tert*-butylphenol) on the respiratory tract. Therefore, the substance has not been designated with “Sa” (for substances which cause sensitization of the airways).

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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