The MAK-Collection for Occupational Health and Safety

GMS PUBLISSO ZB MED-Publikationsportal Lebenswissenschaften

1-Decanol

MAK Value Documentation – Translation of the German version from 2017

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)*

Keywords

1-decanol; irritation; toxicity; developmental toxicity; maximum workplace concentration; MAK value; peak limitation; read-across

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated 1-decanol [112-30-1] to derive a maximum concentration at the workplace (MAK value), considering all toxicity end points. Critical effects are irritation and the tumour-promoting potential on the skin. Neither appropriate data in humans nor inhalation or oral studies of 1-decanol with animals are available for derivation of a MAK value. An 8-week feeding study in Wistar rats with the structurally related 1-dodecanol resulted in a NOAEL of 100 mg/kg body weight and day. The same NOAEL is assumed for 1-decanol. From this NOAEL, the concentration in workplace air was calculated according to the Commission's procedure to be 245 mg 1-decanol/m^3. However, as 1-decanol is irritating and there are no studies of effects in the respiratory tract, a comparison with structurally-related substances is indicated as well. The RD_{50} values of 45 ml/m^3 and 50 ml/m^3 for 2-ethylhexanol and 1-octanol, respectively, are rather similar, which can also be assumed for 1-decanol. Because of its similar irritating potency, the MAK value for 1-decanol has been established at 10 ml/m^3 in analogy to 2-ethylhexanol. As local effects are critical, the substance is assigned to Peak Limitation Category I. The excursion factor of 2 is set in analogy to 2-ethylhexanol. From a synopsis of all data, 1-decanol is classified in Pregnancy Risk Group C, despite the small difference between MAK value and NOAEC of 15 ml/m^3 for developmental toxicity. 1-Decanol is not mutagenic in bacteria. There are no long-term studies with 1-decanol. Papillomas, squamous cell carcinomas and severe skin irritation occurred after 60-week application to the skin of the mouse following initiation with 7,12-dimethylbenz[*a*]anthracene. The maximum skin absorption of 10 mg is less than 25% of the systemically tolerable amount of 660 mg which is taken up by inhalation at the MAK value. There are no positive clinical findings of contact sensitization from 1-decanol, nor are such effects expected from the structure and the comparison with homologous alcohols. Data for sensitization of the airways are not available.

Citation Note:
Hartwig A, MAK Commission. 1-Decanol. MAK Value Documentation – Translation of the German version from 2017. MAK Collect Occup Health Saf. 2022 Jun;7(2):Doc029. https://doi.org/10.34865/mb11230kske7_2or

Manuscript completed:
26 Feb 2016

Publication date:
29 Jun 2022

MAK value (2016)	**10 ml/m³ (ppm) ≙ 66 mg/m³**
Peak limitation (2016)	**Category I, excursion factor 1**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2016)	**Pregnancy Risk Group C**
Germ cell mutagenicity	–
BAT value	–
Synonyms	caprinic alcohol *n*-decyl alcohol
Chemical name	decan-1-ol
CAS number	112-30-1
Structural formula	$H_3C–(CH_2)_9–OH$
Molecular formula	$C_{10}H_{22}O$
Molar mass	158.28 g/mol
Melting point	7 °C (ECHA 2016 b)
Boiling point	231.6 °C (ECHA 2016 b)
Density at 20 °C	0.83 g/cm³ (ECHA 2016 b)
Vapour pressure at 25 °C	0.001 hPa (ECHA 2016 b)
log K_{OW}	4.5 (ECHA 2016 b)
Solubility at 20 °C	21.1 mg/l water (ECHA 2016 b)
1 ml/m³ (ppm) ≙ 6.568 mg/m³	**1 mg/m³ ≙ 0.152 ml/m³ (ppm)**
Stability	decomposes at > 400 °C (EFSA 2010)
Production	technical synthesis, for example via oxo process (Rowe and McCollister 1982)
Purity	≥ 96% (EFSA 2010)
Impurities	no data
Uses	growth regulator for tobacco plants (EFSA 2010); in the production of perfumes, plasticizers, detergents, antifoaming agents, lubricants, elastic plastics (NLM 2016)

Note: The substance can occur simultaneously as vapour and aerosol.

As the dataset available for the substance is very limited, the evaluation draws upon studies that investigated the structurally similar substances 2-ethylhexanol, 1-octanol and 1-dodecanol.

1 Toxic Effects and Mode of Action

Undiluted 1-decanol caused slight irritation in test persons after a single application. After multiple applications, however, severe irritation was observed. 1-Decanol induced severe irritation in rabbit eyes.

No treatment-related effects were determined in pregnant rats after inhalation exposure to 1-decanol at a concentration of 100 mg/m^3. No effects were induced by 1-decanol in mice, even after dermal application for 60 weeks at a dose of 200 mg/kg body weight and day.

In rats, inhalation exposure to 1-decanol during pregnancy at a concentration of 100 mg/m^3 did not induce noticeable changes in the number of resorptions and in the foetal weights. No skeletal or visceral malformations were observed upon examination on gestation day 20.

There are no reliable clinical findings or data from animal studies available for 1-decanol that allow the derivation of contact sensitizing effects.

Salmonella mutagenicity tests carried out with 1-decanol yielded negative results.

Carcinogenic effects were not observed after dermal application of 1-decanol at a dose of 200 mg/kg body weight and day 3 times a week over a period of 60 weeks. Following intraperitoneal initiation with 7,12-dimethylbenz[*a*]anthracene, dermal application of 1-decanol for 60 weeks at a dose of 200 mg/kg body weight and day induced tumour-promoting effects. No long-term studies of carcinogenicity are available.

2 Mechanism of Action

There are no data available.

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

There are no studies available that investigated exposure to 1-decanol by inhalation or oral administration. In vivo and in vitro studies of the absorption of 1-decanol through the skin are available.

After epicutaneous application of undiluted, radioactively-labelled 1-decanol to hairless mice, 8% of the applied radioactivity was absorbed within 24 hours. However, these data are not suitable for a quantitative assessment of dermal absorption because of the marked irritation induced by 1-decanol. The amount absorbed after the application of undiluted 1-decanol solutions depended upon the concentration and the type of solvent. The highest amount absorbed following application of a 0.5% 1-decanol solution (equivalent to 5 g/l) in squalene was about 27% of the administered dose. At this dose, at most slight irritation was observed (Iwata et al. 1987). Fluxes of 67.5 µg/cm^2 in 24 hours and 2.81 µg/cm^2 and hour were determined following application of 100 µl of a solution to a skin surface area of 2 cm^2. On the basis of this flux, 5.6 mg of the substance would be absorbed after 1-hour application to 2000 cm^2 of skin. As 1-decanol is more soluble in squalene than in water, it is probable, however, that less of the substance is absorbed from a saturated aqueous solution, which is the standard used for assessment purposes.

An in vitro study with human skin determined an absorption potential of 60% of the applied dose after occlusive application of an aqueous solution of radioactively-labelled 1-decanol (concentration: 2.5 mg/ml) for 8 hours. A flux of 23 µg/cm^2 in 8 hours corresponding to 2.9 µg/cm^2 and hour was calculated using the data for the volume of the solution applied (10 µl) and the area of skin (0.64 cm^2) (Buist et al. 2010). Under standard conditions (surface area of exposed skin: 2000 cm^2, duration of exposure: 1 hour), 5.8 mg would be absorbed. However, it should be taken into consideration that the concentration of the test solution was about 100 times higher than the solubility of the substance in water (0.021 mg/ml). Assuming that the permeability coefficient Kp is largely independent of the concentration, which is

confirmed by the cited publication, the amount absorbed from a saturated aqueous solution under standard conditions at the calculated flux has probably been overestimated.

In vitro studies investigated the penetration of 1-decanol through porcine skin by applying a solution of 1-decanol in ethanol/water (v/v 9:1). The amount of 1-decanol applied was 260 µg/cm^2. After 4 hours, the systemically available doses were determined to be about 20 µg/cm^2 (evaporation possible) and 45 µg/cm^2 (evaporation prevented), depending on whether measures were taken to prevent the evaporation of the applied solution (Berthaud et al. 2011). For conditions permitting evaporation, which more closely reflect the actual conditions at the workplace, a flux of 5 µg/cm^2 and hour is therefore calculated and under standard conditions (2000 cm^2, duration of exposure 1 hour) 10 mg of the substance is absorbed. As 1-decanol is more soluble in ethanol/water than in pure water and the properties of ethanol may enhance penetration, the amount absorbed from a saturated aqueous solution under standard conditions at the calculated flux has again probably been overestimated.

3.2 Metabolism

The primary aliphatic alcohols are oxidized mainly via the aldehyde, first to the respective carboxylic acid, which then undergoes further degradation, for example by lipid metabolism (IFA 2015).

4 Effects in Humans

There are no data available for reproductive toxicity, genotoxicity and carcinogenicity.

4.1 Single and repeated exposures

There are no data available.

As regards data for the structurally similar **2-ethylhexanol,** the supplement published in 2006 includes a detailed discussion of the local effects of irritation induced in humans. Severe irritation was observed in test persons exposed to 2-ethylhexanol at a concentration of 50 ml/m^3 (Greim 2006 b, available in German only). The increased frequency of eyelid closure determined in test persons was used as a physiological marker of sensory irritation for the derivation of the MAK value. When the benchmark dose (BMD) and the lower confidence limit (BMDL) were calculated on the basis of an increase in the frequency of eyelid closure by one standard deviation of the control value, a BMDL of 14.7 ml/m^3 was determined for 2-ethylhexanol (Hartwig 2012, available in German only).

4.2 Local effects on skin and mucous membranes

4.2.1 Skin

Undiluted 1-decanol induced slight irritation of the skin in Asian, but not in European test persons after occlusive exposure for 4 hours (Robinson 2000, 2001, 2002; Robinson et al. 1998). However, severe irritation was observed after the undiluted substance was applied to the skin multiple times in succession without being removed (75 mg of 1-decanol applied intermittently over a period of 3 days) (no other details; IFA 2015).

In other studies, undiluted 1-decanol induced skin irritation in 24 of 159 test persons after occlusive application for 4 hours. The control, a 20% aqueous solution of sodium lauryl sulfate, produced a reaction in 95 of 159 test persons. Irritant reactions to **1-octanol** or **1-dodecanol** were observed in 5 of 28 test persons in each case. None of the 29 test persons reacted to **tetradecanol** (Basketter et al. 2004).

In a comparative study with the application of 50% formulations of C6 to C18 alcohols in petrolatum for 24 hours, 1-decanol induced slight irritation (grade 3 on a scale of 1 to 5) in some of the 4 test persons (no other details). The ef-

fects were somewhat more severe than those induced by the C8 and C12 homologues (grade 2), while hardly any skin irritation (grade 1) was induced by the longer chain C14, C16 and C18 compounds (Kästner 1977).

Two studies reported that undiluted **1-octanol** caused slight irritation in the 4-hour exposure-chamber test. Determinations were taken 24, 48 and 72 hours after the end of exposure and yielded positive reactions in 4 of 27 and in 5 of 28 test persons, respectively (no other details) (Greim 2003 a).

Summary: Undiluted 1-decanol induced slight irritation in test persons after single applications, and severe irritation after multiple applications.

4.2.2 Eyes

In a study with 26 test persons, the probability of detecting 1-decanol based on eye irritation after 20 exposures to a 1-decanol concentration of 4.5 ml/m^3 lasting 6 seconds each was calculated to be 40%. Therefore, the findings for eye irritation were inconsistent (Cometto-Muñiz et al. 2007).

After short-term exposures (1 to 3 seconds) to **1-octanol** vapour at a concentration of 50 ml/m^3, 5 men and 5 women reported irritation of the eyes and anosmic persons experienced a sharp pain in the nasal mucosa. However, this study is of only limited relevance for workplace exposure because of the shortness of the exposure period (Greim 2003 a).

Summary: Eye irritation was not consistently induced in test persons exposed to 1-decanol concentrations (vapour) of up to 4.5 ml/m^3.

4.3 Allergenic effects

After topical treatment with various formulations over a 2-year period, a 68-year-old female patient with ulcus cruris and tinea pedis developed erythematous, vesicular skin lesions on her foot. Positive reactions were produced in patch tests with all 3 formulations used at that time. In addition, the patient reacted to patch testing with ethanol (5% in water) and with 30% formulations of both **1-hexadecanol** (cetyl alcohol) and **1-octadecanol** (stearyl alcohol) in petrolatum, but not with purified 1-octadecanol (purity 96% to 99%). In additional tests with possible contaminants, reactions were obtained with **oleyl alcohol** (30% in petrolatum) and 1-decanol (5% in petrolatum), but not with **1-dodecanol** (lauryl alcohol, 20% in petrolatum) and **1-tetradecanol** (myristyl alcohol, 5% in petrolatum). No other data were provided for the test protocol used, the time points of the determinations and the severity of the reactions (Ishiguro and Kawashima 1991).

A male patient with a lower limb amputation developed weeping skin lesions on the amputation stump that continued to spread in spite of being treated with formulations containing erythromycin and gentamicin. A positive reaction was obtained in patch tests with the combination ointment containing betamethasone and gentamicin used by the patient. Additional patch tests with the ingredients of the ointment produced 2+ reactions to the ointment base and to both 30% and 10% **1-hexadecanol** and a 1+ reaction to 5% 1-hexadecanol in petrolatum. However, no reaction was produced in patch tests with 1.24 molar formulations (equivalent to formulations with 30% 1-hexadecanol and 19.6% 1-decanol, respectively) of individual, highly purified C10 to C20 alcohols (Komamura et al. 1997).

In a study of 32 patients who produced an initial reaction to lanolin alcohols, lanolin alcohol ointment or an emulsifying ointment, 24 patients reacted to undiluted lanolin alcohol ointment and 24 to 30% lanolin alcohol in petrolatum. Separate tests were carried out with 30% formulations of longer-chained alcohols in petrolatum as possible constituents of lanolin alcohol. Of the 3 tested patients, all reacted also to 1-decanol (purity 98%) and 2 patients to **1-dodecanol** (purity 99%). One patient reacted also to **1-tetradecanol** (purity 96%), but none produced a reaction to **1-hexadecanol** (purity 99%), **1-octadecanol** (purity 99%) or **1-eicosanol** (arachidyl alcohol, purity 99%). None of 5 test persons who were sensitized to lanolin reacted to **1-octanol**. One of the 25 control persons reacted to 1-decanol and 2 to **1-dodecanol**. The lanolin or lanolin alcohol formulations that yielded positive results contained only traces or about 0.1% of 1-decanol and **1-dodecanol**, respectively, and maximum amounts of about 3.4% **1-tetradecanol** (Würbach et al. 1993).

An earlier study tested different long chain aliphatic alcohols in 1664 consecutive patients. Fifteen and 22 patients produced reactions to 5% 1-decanol in petrolatum/olive oil and to 10% 1-decanol in petrolatum, respectively. Reactions were obtained with 5% formulations of **1-octanol**, **1-dodecanol** and **1-tetradecanol** in 11, 4 and 9 patients, respectively, while 15 and 21 patients produced a reaction to 10% formulations of C12 and C14 alcohols, respectively. Only 2 of the 1664 patients reacted to 30% **1-hexadecanol** in petrolatum. The authors pointed out that the C8 to C14 alcohols are primarily irritants and the reactions observed are often impossible to differentiate from "real" eczematous reactions (Hjorth and Trolle-Lassen 1963). In a commentary to these findings, it was stated that 10% formulations of these alcohols, in particular **1-dodecanol**, often produce irritant reactions in patch tests (Kligman 1983). In studies carried out at a later time by the Information Network of Departments of Dermatology (IVDK) and the dermatological clinics in Göttingen and Odense using a 10% test formulation, a correspondingly high number of questionable findings or findings of irritation were obtained with **1-tetradecanol** in up to half of the persons tested. 1-Decanol and **1-dodecanol** were not investigated (Geier et al. 2006 a, b).

In a maximization test with 25 test persons, a 3% formulation of 1-decanol in petrolatum (no other details) did not cause sensitization (Opdyke 1973).

In a maximization test with 25 test persons, a 2% formulation of **1-octanol** in white petrolatum (no other details) did not provide evidence of allergenic effects. The tested concentration did not induce irritation (Greim 2003 a).

In a study of 51 persons who were sensitized to lanolin alcohols, 5 of the sensitized persons produced a weakly positive reaction (erythema and papules) and 4 others a marked reaction (erythema, infiltrates and papulovesicles) to a 30% formulation of **1-dodecanol** in petrolatum. The authors concluded that free fatty alcohols and in particular 1-dodecanol play a crucial role in the development of allergic reactions to lanolin (Auth 1981; Auth et al. 1984). As a result of the emulsifying properties of longer chain alcohols and clinical experiences with similar substances such as **1-tetradecanol** (Geier et al. 2006 a, b), this highly concentrated test formulation is expected to have irritant properties even under occlusive conditions. Therefore, the findings should be interpreted as very probably also irritant effects. However, another explanation is that the reactions were caused by contaminants in the test formulation.

Maximization or patch tests carried out in patients with healthy skin and in different patient collectives did not provide any evidence that **1-dodecanol** induces allergenic effects (Greim 2006 a).

Summary: There are no valid positive clinical findings that provide evidence that 1-decanol has contact sensitizing potential. The reactions discussed in the literature are only of limited relevance for the evaluation because of the high test concentrations used and the expected irritant effects after occlusive application for 24 to 48 hours. No evidence of allergenic effects can be derived from structure–effect comparisons or by drawing upon the findings obtained with homologous alcohols.

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

In a study from 1977, rats were exposed whole-body to 1-decanol at a concentration of 71 mg/l (71 000 mg/m^3) for 1 hour. The animals were hypoactive or ataxic during exposure and wheezing and salivation were observed. Gross-pathological examination revealed slight to moderate congestion in the lungs of all animals (ECHA 2016 b).

LD_{50} values of 2050 mg/m^3 (gravimetric) and 11 460 mg/m^3 (nominal) were determined for rats within 14 days after 4-hour exposure. After exposure, hypoactivity, hunched posture, changes in breathing sounds and nasal discharge were observed. The surviving animals recovered after 7 days. Gross-pathological examination did not reveal any changes in the organs (ECHA 2016 b).

All rats survived whole-body exposure to a mixture of *n*-decyl alcohol and secondary decyl alcohol at a concentration of 905 mg/m^3 for 6 hours (Treon 1963) or to 10% 1-decanol in ethanol for 2 hours (ECHA 2016 b).

Studies carried out in mice with structurally similar substances determined RD_{50} values of 50 ml/m^3 for **1-octanol** (Muller and Greff 1984) and 45 ml/m^3 for **2-ethylhexanol** (Greim 2003 b).

5.1.2 Oral administration

The LD_{50} for 1-decanol was above 6000 mg/kg body weight after oral administration in rats and mice (Treon 1963).

5.1.3 Dermal application

The dermal LD_{50} for 1-decanol was above 5000 mg/kg body weight in rats and between 2000 and 4000 mg/kg body weight in rabbits (ECHA 2016 b). The dermal LD_{50} for a mixture of *n*-decyl alcohol and secondary decyl alcohol was determined to be 3560 mg/kg body weight in rabbits and above 10 000 mg/kg body weight in guinea pigs (Treon 1963).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

Inhalation exposure of 15 pregnant Sprague Dawley rats to 1-decanol vapour at a concentration of 100 mg/m^3 for 6 hours a day for 19 days did not lead to treatment-induced effects on feed and water consumption or body weights. Examinations carried out on gestation day 20 did not determine unusual findings in the foetuses (see Section 5.5). A higher vapour concentration could not be achieved in this study as a result of the low vapour pressure of 1-decanol. Neither the nose nor the nasal mucosa was examined (Nelson et al. 1990 a, b).

5.2.2 Oral administration

No studies with repeated oral administration have been carried out with 1-decanol.

In a feeding study with **1-dodecanol**, groups of 12 male and 12 female Wistar rats were given 1-dodecanol (purity 99%) concentrations of 0, 1500, 7500 or 30 000 mg/kg feed (doses of about 0, 100, 500 and 2000 mg/kg body weight and day, respectively) for 8 weeks. No changes were observed as regards body weights, feed consumption and organ weights or in the gross-pathological and microscopic examinations. Blood tests were performed only in the males and revealed a dose-dependent decrease in the leukocyte count at doses of 500 and 2000 mg/kg body weight and day and in the triglyceride levels at 2000 mg/kg body weight and day. The findings of the differential blood count did not reflect these changes. As a result of the reduced leukocyte count, the NOAEL (no observed adverse effect level) of this study was 100 mg/kg body weight and day (Greim 2006 a).

5.2.3 Dermal application

In a 60-week initiation/promotion study in groups of 30 female mice, severe irritation was induced by dermal application of 1-decanol 3 times a week at a dose of 200 mg/kg body weight and day. Local effects, such as hair loss and erythema, were most severe between weeks 6 and 12. No systemic effects were observed (Sicé 1966).

In a 90-day study carried out according to OECD Test Guideline 411, a mixture of alcohols containing about 50% 1-decanol and about 45% **1-octanol** was applied semi-occlusively to the dorsal skin of groups of 10 male and 10 female Sprague Dawley rats on 5 days a week. In each case, the solution was wiped off after 6 hours with a paper towel moistened with water. The alcohol mixture was applied in doses of 0, 100, 300 or 1000 mg/kg body weight and day. The animals emitted cries, fought during the exposure (no other details) and were oversensitive to the touch. Marked skin irritation was observed at the low dose of 100 mg/kg body weight and day and above, which intensified as treatment continued. The reduced body weights and the reduced feed consumption were attributed to irritation. The effects on the

leukocyte count and albumin and globulin levels (no other details) were regarded as a response to the inflammation of the skin. Increased adrenal gland weights, which were not accompanied by pathological changes, were probably the result of stress induced by the irritation. The study determined a LOAEL (lowest observed adverse effect level) of 100 mg/kg body weight and day for local irritation and the secondary systemic effects that developed as sequelae (ECHA 2016 b, d).

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

In a study carried out in 3 New Zealand White rabbits according to OECD Test Guideline 404, the irritation indices were determined after semi-occlusive application of 0.5 ml undiluted 1-decanol to the shaved skin for 4 hours. The mean erythema scores for each animal after 24, 48 and 72 hours were 1.7, 2.0 and 2.0 on a scale with a maximum score of 4. Oedema was not observed. Symptoms of irritation were no longer detectable after 10 days. 1-Decanol was not assessed as irritating in this study (ECHA 2016 b).

Another study carried out according to OECD Test Guideline 404 with semi-occlusive application of undiluted 1-decanol (purity 98.8%) to 4 rabbits for 4 hours was reported. A mean irritation index of 3.33 (of a maximum score of 8) was calculated for erythema and oedema 24, 48 and 72 hours after patch removal. The mean scores determined for each of the 4 animals after 24, 48 and 72 hours were 2.3, 2.3, 2.2 and 1.8 for erythema and 2.0, 0.8, 1.0 and 0.8 for oedema. The effects had weakened by the end of the 7-day observation period and skin desquamation was observed in all animals. 1-Decanol was assessed as irritating to the skin (Bagley et al. 1996; ECHA 2016 b).

Following semi-occlusive application of undiluted 1-decanol to the shaved skin of 3 female New Zealand White rabbits for 4 hours, erythema and mild oedema were observed at all application sites 24 hours after patch removal. These effects gradually subsided and were no longer detectable after 10 days. The mean irritation index, determined on the basis of the readings taken after 60 minutes and after 24, 48 and 72 hours, was 2.8 (graded according to the scale proposed by Draize; no other details). 1-Decanol was described as not irritating to the skin (ECHA 2016 b).

After occlusive application of a 50% formulation of 1-decanol in petrolatum (no other details) to the shaved skin for 24 hours, moderate irritation (grade 4; scale 1 to 5) was observed in rabbits and only slight irritation (grade 2) in guinea pigs and hairless mice. Similar effects were observed when tests were carried out with **C12** and **C14 alcohols** (Kästner 1977). Severe irritation was reported after application of an undiluted mixture of ***n*-decyl alcohol** and secondary decyl alcohol (no other details) for 24 hours (Opdyke 1973; Treon 1963).

Summary: In rabbits, undiluted 1-decanol induced only slight irritation to the skin, if any at all, after semi-occlusive application for 4 hours. Moderate irritation was observed only after occlusive application of a 50% formulation of 1-decanol in petrolatum for 24 hours, while severe irritation was detected following the application of an undiluted mixture of *n*-decyl alcohol and secondary decyl alcohol.

5.3.2 Eyes

In a Draize test carried out with 3 New Zealand White rabbits, the instillation of 0.1 ml undiluted 1-decanol into the conjunctival sac induced corneal opacity, iritis, conjunctivitis and conjunctival oedema in all 3 animals within 1 hour; maximum irritation was reached after 24 hours with a maximum mean score of 28.3. The scores determined for the 3 animals were 1, 1 and 1 (24 and 48 hours) and 0, 0 and 0 (72 hours) for corneal opacity, 1, 1 and 1 (24 and 48 hours) and 1, 0 and 0 (72 hours) for effects on the iris and 3, 3 and 2 (24 hours), 2, 2 and 2 (48 hours) and 2, 1 and 1 (72 hours) for conjunctival redness. The scores determined for conjunctival oedema were 2, 2 and 2 after 24 hours, 1, 1 and 1 after 48 hours and 1, 1 and 0 after 72 hours. After 7 days, no symptoms of irritation were detected in the eyes of the animals. 1-Decanol was assessed as irritating to the eyes (ECHA 2016 b).

In a study carried out according to OECD Test Guideline 405, 0.1 ml undiluted 1-decanol was instilled once into the conjunctival sac of one eye of 3 New Zealand White rabbits to investigate irritation of the eyes 1, 24, 48 and 72 hours and 7, 14 and 21 days after application. After 24, 48 and 72 hours, the mean irritation index for corneal opacity was 1.23 on a scale with a maximum of 2 (mean score per animal: 2.0, 1.0, 0.7), for effects on the iris 0.56 of a maximum of 1 (mean score per animal: 0.7, 0.3, 0.7), for conjunctival redness 1.77 of a maximum of 3 (mean score per animal: 2.7, 1.3, 1.3) and for conjunctival oedema 0.63 of a maximum of 2 (mean score per animal: 1.3, 0.3, 0.3). Slight corneal opacity was still noticeable in 1 animal after 7 days and in another after 14 days. After 21 days, no effects were detected in any of the animals. According to the criteria of the Globally Harmonized System of Classification, Labelling and Packaging of Chemicals (GHS), 1-decanol has been assessed as an eye irritant based on the corneal opacity of higher than grade 1 severity that persisted for longer than 7 days (ECHA 2016 b).

The mean scores determined for the structurally similar substance **2-ethylhexanol** were 2.56 on a scale with a maximum of 3 for erythema, 0.78 of a maximum of 4 for conjunctival oedema, 1.44 of a maximum of 4 for corneal opacity and 0.89 of a maximum of 2 for iritis (Greim 2003 b).

In another study of **2-ethylhexanol** carried out according to OECD Test Guideline 405 in 4 New Zealand White rabbits, the mean irritation scores determined after 24, 48 and 72 hours were 1.75 for the cornea, 0.67 for the iris, 2.08 for conjunctival redness and 1.92 for conjunctival swelling. The study did not apply the GHS classification (ECHA 2016 a).

Three studies carried out according to OECD Test Guideline 405 to investigate irritation of the eyes in New Zealand White rabbits found **1-octanol** to be irritating to the eyes according to GHS criteria (ECHA 2016 d).

In a Draize test, the instillation of undiluted **1-dodecanol** and mixtures of 1-dodecanol and 1-tetradecanol in the rabbit eye induced slight irritation (Greim 2006 a).

Summary: Like **2-ethylhexanol** and **1-octanol**, 1-decanol induces irritation of the eyes.

5.4 Allergenic effects

5.4.1 Sensitizing effects on the skin

In a Buehler test, 10 guinea pigs were treated for induction with 0.4 ml of undiluted 1-decanol and for the challenge with 0.4 ml of a 25% formulation of 1-decanol in mineral oil (no other details). 1-Decanol was not found to induce sensitizing effects in this test (ECHA 2016 b).

In an incompletely documented test with intradermal administration that was described as a modified Draize test, 10 guinea pigs were treated for induction with 4 simultaneously administered intradermal injections of 1-decanol (1.9%, no other details). Sensitizing effects were not observed after the challenge treatment 14 days later (0.75% and 10% solutions administered by intradermal injection and open epicutaneous application, respectively; no other details). Reactions were obtained only after a second induction treatment (no other details). The authors classified 1-decanol as weakly sensitizing (Sharp 1978). However, the number of animals that produced positive reactions and the severity of the reactions were not documented.

In a study carried out according to OECD Test Guideline 406 with **1-dodecanol**, 10 guinea pigs were treated for intradermal induction (with 3% 1-dodecanol in paraffin oil) followed 7 days later by epicutaneous induction (with 50% 1-dodecanol in paraffin oil). The epicutaneous challenge treatment (with 3% and 10% 1-dodecanol in paraffin oil) was performed 21 days after intracutaneous induction. 1-Dodecanol was not sensitizing to the skin in this test system (ECHA 2016 c).

Summary: Contact sensitizing effects cannot be derived for 1-decanol on the basis of the findings available from animal studies.

5.4.2 Sensitizing effects on the airways

There are no data available for sensitizing effects on the airways.

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

There are no studies that investigated fertility after the administration of 1-decanol.

In a 1-generation study, male and female Wistar rats were given **1-dodecanol** (purity 99%) concentrations of 0, 1500, 7500 or 30000 mg/kg feed (1-dodecanol doses of about 0, 100, 500 or 2000 mg/kg body weight and day) for 8 weeks. No statistically significant changes were noted in the number of pregnancies, the length of the gestation period, the number of offspring per litter, the weight and sex ratio of the offspring and their viability up to postnatal day 5 over the 8-week examination period (Greim 2006 a).

5.5.2 Developmental toxicity

5.5.2.1 Inhalation

Daily inhalation exposure of 15 pregnant Sprague Dawley rats to 1-decanol at a concentration of 100 mg/m^3 (15 ml/m^3, the highest possible vapour concentration at room temperature) for 6 hours a day did not induce treatment-related effects during the first 19 days of gestation. Feed consumption, water consumption and body weights were monitored (see also Section 5.2.1) and on gestation day 20 the number of resorptions and foetal weights were determined and the foetuses were examined for skeletal and visceral malformations (Nelson et al. 1990 a, b). The study did not use a separate group of concurrent control animals. However, findings in the control animals used by the same group of authors for other studies carried out in a similar time period (Nelson et al. 1990 a, b) serve as general reference points for the foetotoxic parameters of untreated animals. The study was regarded as valid because of the protocol used and the good quality of the documentation.

No treatment-related effects were observed in a similar study carried out with **1-octanol**. In this study, 15 pregnant Sprague Dawley rats were exposed by inhalation to 1-octanol concentrations of 0 or 400 mg/m^3 (about 0 or 75 ml/m^3, respectively, for 7 hours a day) during the first 19 days of gestation. Feed and water consumption and the body weights of the dams, the number of resorptions, the foetal weights and skeletal and visceral malformations (no other details) were investigated (Nelson et al. 1990 a, b).

5.5.2.2 Oral administration

None of the available studies investigated developmental toxicity induced by oral administration of 1-decanol.

An aqueous emulsion of **1-octanol** given to groups of 8 to 10 Wistar rats in gavage doses of 0, 130, 650, 975 or 1300 mg/kg body weight and day from gestation days 6 to 15 induced prostration and lateral position, unsteady gait, salivation, ruffled fur, nasal discharge and pulmonary inflammation in the treated animals. In the low dose group, the effects were only mild. Effects on uterine and placental weights, the number of live births or the foetal weights were not observed in any of the dose groups. There was no evidence of teratogenicity (no other details) (Greim 2003 a).

5.6 Genotoxicity

5.6.1 In vitro

In Salmonella mutagenicity tests with the Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538, 1-decanol was not found to be mutagenic up to the cytotoxicity threshold of 500 µg/plate in the presence or absence of a metabolic activation system (ECHA 2016 b).

Also **1-octanol** (Greim 2003 a) and **1-dodecanol** (Greim 2006 a) were not found to be mutagenic in bacteria.

1-Octanol induced spindle abnormalities (c-mitosis and aneuploidy) in V79 cells at concentrations of about 0.1 mM and above. Their development was attributed to a non-specific physical mechanism based on the distribution of lipophilic compounds in hydrophobic cell compartments (Greim 2003 a).

5.6.2 In vivo

There are no studies of genotoxicity in vivo available for 1-decanol.

CFW mice were given **1-dodecanol** by gavage in single doses of 0 or 5000 mg/kg body weight. Examinations of polychromatic erythrocytes in the bone marrow carried out after 24, 48 and 72 hours did not determine an increase in the number of cells with micronuclei or cytotoxicity (Greim 2006 a).

5.7 Carcinogenicity

There are no long-term studies available with 1-decanol.

In a 60-week initiation-promotion study in Swiss mice, dermal application of 1-decanol at a dose level of 200 mg/kg body weight and day following intraperitoneal initiation with 7,12-dimethylbenz[*a*]anthracene (5 µg in 0.1 ml acetone) was found to promote the development of skin tumours. 1-Decanol led to severe irritation at the application site. 1-Decanol did not induce skin tumours without prior initiation with 7,12-dimethylbenz[*a*]anthracene. When exposure was preceded by initiation, papillomas developed in 3 of 30 mice, which evolved into squamous cell carcinomas in 2 animals (see Table 1).

Studies carried out with other alkanols using the same treatment protocol and the same dose levels reported papilloma incidences of 1/30 for **1-octanol** and 2/30 for **1-dodecanol**. These did not evolve into squamous cell carcinomas (Gilbert and Sicé 1960; Sicé 1966).

Tab. 1 Initiation-promotion study

Species, strain, number per group	Exposure	Findings	References
mice, Swiss, 30 ♀	**60 weeks,** **initiation**: 1 × 5 µg 7,12-dimethylbenz[*a*]-anthracene, intraperitoneal, **promotion**: 4 mg 1-decanol/20 µl cyclohexanol (200 mg 1-decanol/kg body weight), dermal, 3 ×/week; controls: without initiation and 1-decanol	**1 × 5 µg 7,12-dimethylbenz[*a*]anthracene and 180 × 200 mg 1-decanol/kg body weight**: 6/30 ♀ with papillomas, first after 25 weeks, 2 papillomas evolved into squamous cell carcinomas; application caused severe irritation, hair loss and erythema most severe between week 6 and 12; no systemic effects; 1-decanol did not induce skin tumours without initiation	Gilbert and Sicé 1960; Sicé 1966

6 Manifesto (MAK value classification)

The critical effects of 1-decanol are irritation of the eyes and the skin tumour-promoting potential.

MAK value. There are no human data available that are suitable for the derivation of a MAK value, and no inhalation studies that are relevant to the evaluation or animal studies with oral administration of 1-decanol. An 8-week feeding study in Wistar rats with the structurally similar **1-dodecanol** determined a NOAEL of 100 mg/kg body weight and day based on the reduced leukocyte count at 500 mg/kg body weight and day (Greim 2006 a). Therefore, it is assumed that the NOAEL of 1-decanol for systemic effects is also in this dose range. The following toxicokinetic data are taken into consideration for the extrapolation of the assumed NOAEL for 1-decanol of 100 mg/kg body weight and day to a concentration in workplace air: the corresponding species-specific correction value for the rat (1:4), the body weight (70 kg) and the respiratory volume (10 m^3) of the person, the assumed 100% absorption both by oral routes and by inhalation and the 5 days per week exposure at the workplace (7:5). The concentration calculated from this for 1-decanol is 245 mg/m^3 (37 ml/m^3).

However, as 1-decanol was found to cause irritation of the eyes, but there are no studies available that investigated irritation of the respiratory tract, the irritant effects make it necessary to draw upon findings from structurally related substances for the evaluation (see Table 2). The severity of the irritation induced by **2-ethylhexanol** and **1-octanol** is very similar to that induced by 1-decanol. In addition, the RD_{50} values, which are known only for **2-ethylhexanol** and **1-octanol**, are very close at 45 ml/m^3 and 50 ml/m^3, respectively. A MAK value of 10 ml/m^3 was derived for **2-ethylhexanol** based on the increased frequency of eyelid closure observed in test persons. As the severity of the irritation induced by the substances is quite similar, a MAK value of 10 ml/m^3 has been derived for 1-decanol in analogy to that for **2-ethylhexanol**.

On the basis of the extrapolated 1-decanol concentration of 245 mg/m^3 (37 ml/m^3) and the application of a factor of 2 both for the possible intensification of the effects over time and for the extrapolation of the data from animal studies to the human, taking into consideration the preferred value approach, a value of 10 ml/m^3 has been determined also for systemic effects.

Tab. 2 Comparison of the physico-chemical data and the irritation induced by structurally similar alkanols

Alkanol	CAS number	Solubility in water	Vapour pressure [hPa]	Irritation		RD_{50} mouse	References
				skin	eyes[a)]		
2-ethylhexanol	104-76-7	900 mg/l	0.93	mild to moderate	severe	45 ml/m^3 (Alarie et al. 2001)	ECHA 2016 a
1-octanol	111-87-5	107 mg/l	0.03	mild to moderate	severe	50 ml/m^3 (Muller and Greff 1984)	ECHA 2016 d
1-decanol	112-30-1	21 mg/l	0.001	mild	severe	no data	ECHA 2016 b
1-dodecanol	112-53-8	1 mg/l	0.001	mild to moderate	none to moderate	no data	ECHA 2016 c

[a)] Classification according to GHS (ECHA 2016 a, b, c, d)

Peak limitation. As the MAK value for 1-decanol was derived on the basis of irritant effects, the substance has been classified in Peak Limitation Category I. There are no data available for irritation in humans. An excursion factor of 1 has been set in analogy to that for 2-ethylhexanol.

Prenatal toxicity. In a study of pregnant Sprague Dawley rats exposed by inhalation to a 1-decanol concentration of 100 mg/m^3 for 19 days, no treatment-related effects were observed in the dams and foetuses. This study, which is regarded as valid, used the maximum possible vapour concentration of 1-decanol of 100 mg/m^3. Higher levels of exposure to vapour are therefore not to be assumed for the workplace. In addition, the actual NOAEC (no observed adverse effect concentration) may be much higher, as shown by the findings determined with homologous substances.

In a study investigating the developmental toxicity induced by 1-octanol, no foetotoxic effects or developmental toxicity were observed up to the highest dose tested of 1300 mg/kg body weight and day (≙ about 2300 mg/m³) (Greim 2003 a). In a 1-generation study in Wistar rats, 1-dodecanol was not found to induce adverse effects in the dams or offspring up to the highest dose tested of about 2000 mg/kg body weight and day (≙ about 4900 mg/m³) (Greim 2006 a). As a result of the high NOAELs determined for the structurally-related substances and after reviewing all the available data, 1-decanol has been classified in Pregnancy Risk Group C in spite of the small margin between the MAK value and the experimentally determined NOAEC for developmental toxicity, which is assumed to be much higher in reality.

Carcinogenicity and germ cell mutagenicity. 1-Decanol was not mutagenic in bacteria. There are no other studies of genotoxicity and long-term studies of carcinogenicity with 1-decanol. Skin tumours were not induced in mice after epicutaneous application for 60 weeks. Papillomas, squamous cell carcinomas and severe skin irritation were observed only after initiation with 7,12-dimethylbenz[*a*]anthracene. In the absence of data for carcinogenicity and, as mutagenic effects are not to be expected for structural reasons, 1-decanol has not been classified in a category for carcinogenic or for germ cell mutagenic substances.

Absorption through the skin. In vivo and in vitro data demonstrated that 1-decanol penetrates through the skin. On the basis of these data, it was determined that an absorbed amount of 10 mg 1-decanol represents the worst-case scenario under standard conditions. Taking into consideration the dermal LD_{50} values of above 2000 mg/kg body weight and the NOAEL for systemic effects of 200 mg/kg body weight and day derived from a study with epicutaneous application of 1-decanol to mice 3 times a week over a period of 60 weeks, it was concluded that the systemic toxicity induced by dermal exposure to the compound is relatively slight. Not enough reliable data are available to compare the absorption of 1-decanol through mouse skin and human skin. Therefore, the NOAEL for dermal effects cannot be used to assess the estimated absorbed amount of 10 mg. The MAK value of 10 ml/m³ (66 mg/m³) was derived primarily on the basis of the irritation induced by the substance; however, systemic effects are also not expected to occur at this level of exposure. An 8-hour exposure at the level of the MAK value corresponds to a systemically tolerable amount of at least 660 mg 1-decanol. With a maximum absorbed amount of 10 mg, absorption through the skin is markedly lower than 25% of this amount. 1-Decanol has therefore not been designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. There are no valid positive clinical findings available for contact sensitizing effects of 1-decanol, as the reactions described in the literature are of only very limited relevance to the evaluation because high test concentrations were used and after occlusive application for 24 to 48 hours irritation is expected to occur. Likewise, on the basis of structure–effect considerations and a comparison with homologous alcohols, contact sensitizing effects are not expected for 1-decanol. In addition, negative findings in a Buehler test did not provide evidence of contact sensitizing effects. Data for sensitizing effects on the respiratory tract are not available. For this reason, 1-decanol has neither been designated with "Sh" nor with "Sa" (for substances which cause sensitization of the skin or 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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