The MAK-Collection for Occupational Health and Safety

GMS PUBLISSO ZB MED-Publikationsportal Lebenswissenschaften

n-Decyl oleate

MAK Value Documentation, supplement – Translation of the German version from 2019

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Keywords

n-decyl oleate; lung; accumulation; maximum workplace concentration; MAK value; developmental toxicity; read-across

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated *n*-decyl oleate [3687-46-5], considering all toxicological end points. Available publications and unpublished study reports are described in detail. As with white mineral oil, inhalation of aerosols of the hardly water-soluble *n*-decyl oleate could result in overload in the lung, inflammatory reactions and microgranulomas. To prevent this overload, a maximum concentration at the workplace (MAK value) of 5 mg/m^3 is derived for the respirable fraction by analogy with white mineral oil and Peak Limitation Category II as well as an excursion factor of 4 are set. There are no developmental toxicity studies and *n*-decyl oleate is assigned to Pregnancy Risk Group D. *n*-Decyl oleate is not genotoxic in bacteria. Carcinogenicity studies are not available. There are no indications of a contact sensitizing potential of *n*-decyl oleate in humans and in animal studies. Skin contact is not expected to contribute significantly to systemic toxicity.

Citation Note:
Hartwig A, MAK Commission. n-Decyl oleate. MAK Value Documentation, supplement – Translation of the German version from 2019. MAK Collect Occup Health Saf. 2021 Sep;6(3):Doc056.
DOI: https://doi.org/10.34865/mb368746kske6_3ad

Manuscript completed:
12 Oct 2017

Publication date:
30 Sep 2021

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MAK value (2018)	**5 mg/m³ R (respirable fraction)**
Peak limitation (2018)	**Category II, excursion factor 4**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2018)	**Pregnancy Risk Group D**
Germ cell mutagenicity	–
BAT value	–
CAS number	3687-46-5
Melting point	−5 °C (ECHA 2017 a)
Boiling point	no data
Density at 20 °C	0.86 g/cm³ (ECHA 2017 a)
Vapour pressure	7.82×10^{-11} hPa (calculated) (ECHA 2017 a)
log K_{OW}	12.44 (calculated) (ECHA 2017 a)
Solubility	not soluble in water (Krop et al. 1997) 370 ng/l at 25 °C (no other details) (ECHA 2017 a)
Stability	no data
Production	esterification of oleic acid with *n*-decyl alcohol
Impurities	a maximum of 2.5% oleic acid (CIR 1982)
Uses	in cosmetics in concentrations of ≤ 0.1%–> 50% (CIR 1982), 0.5%–88% (CIR 2003); as a textile or leather auxiliary

For *n*-decyl oleate documentation is available from 1995 (Greim 1998).

Metal-working fluid concentrates contain amounts of up to 20% *n*-decyl oleate (Hartwig 2014, available in German only). A NOAEC (no observed adverse effect concentration) for skin irritation is not known; after single applications, *n*-decyl oleate was not irritating to the skin of rabbits.

This supplement is based on new studies of repeated administration and reproductive toxicity. It examines whether a MAK value for *n*-decyl oleate can be established. To complete the toxicological profile, studies with the structural analogue isodecyl oleate [59231-34-4] and similar fatty acid esters, such as 2-ethylhexyl oleate [26399-02-0], oleyl oleate [3687-45-4] and 2-octyldodecyl isooctadecanoate [93803-87-3], are also included. The names of these substances are shown in bold print for better clarity.

The supplement is based mainly on the publicly available REACH registration data (ECHA 2017 a).

1 Toxic Effects and Mode of Action

A study in rats with repeated oral administration yielded a NOAEL (no observed adverse effect level) of 1000 mg *n*-decyl oleate/kg body weight and day, the highest dose tested.

n-Decyl oleate is not irritating to the skin and eyes of rabbits.

In Sprague Dawley rats, the NOAEL for effects on fertility for the structural analogue isodecyl oleate was 1000 mg/kg body weight and day and the LOAEL (lowest observed adverse effect level) for developmental and maternal toxicity was 1000 mg/kg body weight and day, based on the increased incidences of post-implantation losses, stillbirths and not viable offspring. Similar effects can be expected with *n*-decyl oleate.

n-Decyl oleate was not found to be mutagenic in Salmonella mutagenicity tests. As studies with the structural analogues 2-ethylhexyl oleate and oleyl oleate did not reveal genotoxic effects in mammalian cells and 2-octyldodecyl isooctadecanoate did not induce micronuclei in the bone marrow of mice, it can be assumed that *n*-decyl oleate is likewise not genotoxic in these test systems.

There are no reliable findings in humans that *n*-decyl oleate has skin sensitizing effects and no positive test results from animal studies. There are no data for sensitizing effects of *n*-decyl oleate on the airways.

2 Mechanism of Action

After inhalation exposure, it is conceivable that **isodecyl oleate** that has entered the lungs is cleaved into oleic acid and isodecyl alcohol. Oleic acid is used in animal experiments as a model substance for the development of the acute respiratory distress syndrome (ARDS) in humans. After intravenous or intratracheal administration of oleic acid or oleic acid suspensions (in albumin or phosphate-buffered saline), for example to rats (Akella et al. 2014; Dickey et al. 1981; Ito et al. 2005), mice (Gonçalves-de-Albuquerque et al. 2012, 2013, 2015), dogs (Henning et al. 1986; Kato et al. 1998; Leeman et al. 1990; Scillia et al. 2001) and pigs (Neumann et al. 2000), lung damage similar to ARDS was induced. ARDS is defined as acute respiratory insufficiency with an initial increase in the permeability of the alveolar and capillary membranes and oedema formation in the alveoli and interstitium (see Gonçalves-de-Albuquerque et al. 2015). However, experiments with intravenous or intratracheal administration are not relevant for occupational exposure. As there are no corresponding inhalation studies with oleic acid, there is no NOAEC for this effect. It is not clear whether oleic acid is released after inhalation of **isodecyl oleate**. For other fatty acids, there are no studies of occupational exposure available. Pharmaceutical products, such as propellant-driven metered-dose inhalers for the inhalation of drugs in which the active ingredient is suspended, are known to contain dissolved excipients such as oleic acid, sorbitan trioleate or lecithin. The oleic acid serves as a suspension stabilizer (Kircher 2003). Assuming that in a metered-dose aerosol the spray volume is 50 µl (for example Fujisawa 2002; TEVA 2008) and assuming that oleic acid makes up a maximum of 1%, the patient would inhale 0.5 µl of oleic acid in a single application. With 1 to 2 single doses 3 to 4 times a day or 4 sprays twice a day (for example Fujisawa 2002), the patient would inhale about 4 µl oleic acid per day. However, the package inserts of many drugs administered in this way do not describe the symptoms of pulmonary oedema, such as shortness of breath, cyanosis, expectoration and coughing (for example Cheplapharm 2008; Hexal 2016).

3 Toxicokinetics and Metabolism

n-Decyl oleate might be cleaved to oleic acid and *n*-decyl alcohol which could be oxidised to the aldehyde or to the carboxylic acid.

4 Effects in Humans

Local effects on skin and mucous membranes

On the inside of the forearms of volunteers, 2-hour application of undiluted *n*-decyl oleate with a plaster (Henkel 1970 b) or application for 30 minutes with simultaneous massaging into the skin of the substance with a glass rod every 30 seconds (Burckhardt test) (Henkel 1970 a) did not cause irritation (Greim 1998).

Allergenic effects

There is only one incompletely documented finding of a positive reaction to a 1% preparation of *n*-decyl oleate in petrolatum in a patch test (no other details). The substance was a component of a moisturizing lotion containing urea, to which the patient produced a 3+ reaction in the patch test (Garcia-Bravo and Mozo 1992).

Four ointment base formulations, each containing up to 5% *n*-decyl oleate, did not cause skin reactions in 402 subjects after single occlusive applications and in 204 subjects in repeated insult patch tests (CIR 1982; Greim 1998).

Likewise, in 103 volunteers who received applications of 0.2 ml of a skin conditioner containing 1% to 5% *n*-decyl oleate (no other details) 3 times a week for 3 weeks in patch tests and were subsequently exposed to a challenge treatment with the undiluted skin conditioner (no other details) 14 days after the final application, no evidence of sensitization was found at the readings after 48 or 96 hours (Greim 1998).

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

There are no data available for *n*-decyl oleate.

5.1.2 Oral administration

In rats, the LD_{50} of *n*-decyl oleate was greater than 2000 mg/kg body weight (Greim 1998), as was that of the structural analogue **isodecyl oleate (**Greim 2001).

5.1.3 Dermal application

The dermal LD_{50} of *n*-decyl oleate was greater than 2000 mg/kg body weight in Wistar rats. Piloerection and/or chromodacryorrhoea (discoloured lacrimation) were observed in all males on day 1 and/or 2. In all females and 3 of 5 males, scales, scabs and focal erythema were seen in the treated skin area during the 15-day observation period. No clinical signs of systemic toxicity were noted in females (ECHA 2017 a).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

There are no data available for *n*-decyl oleate.

5.2.2 Oral administration

In a 4-week study with gavage doses of *n*-decyl oleate of 0, 100, 500 or 1000 mg/kg body weight and day (see Table 1) on 5 days per week, and a subsequent recovery period of 4 weeks, no substance-related effects were found in the 10 male and 10 female Sprague Dawley rats per dose group (Henkel 1987).

In female Sprague Dawley rats given gavage doses of **isodecyl oleate** of up to 1000 mg/kg body weight and day 2 weeks before mating up to 3 days after giving birth, no organ changes were found. During the lactation period there was a body weight loss of 9.4%. The toxic effects on development, such as post-implantation losses, stillbirths or dead pups are described in Section 5.5.2. In the males, no substance-related damage was observed after the administration of **isodecyl oleate** doses of up to 1000 mg/kg body weight and day for 35 days (see Table 1). The NOAEL for the male animals and for females that were not pregnant was therefore 1000 mg isodecyl oleate/kg body weight and day and for lactating dams 300 mg/kg body weight and day (Zschimmer & Schwarz 2013).

Tab. 1 Toxicity studies with repeated oral administration of *n*-decyl oleate and isodecyl oleate

Species	Exposure	Findings	References
***n*-Decyl oleate**			
rats, Wistar, groups of 10 treated ♂ and 10 treated ♀, groups of 5 untreated ♂ and 5 untreated ♀	**28 days**, 0, 100, 500 or 1000 mg ***n*-decyl oleate** (in olive oil)/kg body weight and day, purity not specified, 5 days/week, gavage, recovery period: 28 days	**1000 mg/kg body weight**: **NOAEL**; no effects on body weights, organ weights; no gross-pathological and histological changes	Henkel 1987
Isodecyl oleate			
rats, Sprague Dawley, groups of 5 ♂ and 5 ♀	**14 days**, 0, 100, 300 or 1000 mg **isodecyl oleate** (in corn oil)/kg body weight and day, purity 99%, daily, 7 days/week, gavage	**1000 mg/kg body weight**: **NOAEL**; no effects on body weights, organ weights or after gross-pathological examination of all organs, histopathological examination not carried out	Zschimmer & Schwarz 2012
rats, Sprague Dawley, groups of 10 ♂ and 10 ♀	♂: **35 days**, ♀: **max. 56 days**, 0, 100, 300 or 1000 mg **isodecyl oleate** (in corn oil)/kg body weight and day, purity 77.8% (C_{14}–C_{20}, < 10% per component), daily, 7 days/week, gavage, ♂: start 2 weeks before mating; ♀: start 2 weeks before mating up to 3 days after giving birth	**300 mg/kg body weight**: ♀: **NOAEL**; **1000 mg/kg body weight**: ♀: only during lactation period body weights ↓, for other effects on reproduction, see Sections 5.5.1 and 5.5.2, ♂: **NOAEL**, no effects on spermatogenesis; blood count, clinical chemistry or blood coagulation: no unusual findings; gross-pathological examination: no effects on tongue, trachea, larynx, oesophagus, gastrointestinal tract, adrenal glands, bone marrow, nervous system, spinal cord, brain, heart, kidneys, ureter, bladder, reproductive organs, liver, lungs, lymph nodes, spleen or thyroid gland; organ weights: no effects on testes, epididymis, kidneys, adrenal glands, brain, heart, liver, spleen or thymus; histopathological examination: no unusual findings	Zschimmer & Schwarz 2013

Summary: The study in rats with repeated oral administration yielded a NOAEL of 1000 mg *n*-decyl oleate/kg body weight and day, the highest dose tested. This value is confirmed by the findings for the structurally similar **isodecyl oleate** in male animals and females that were not pregnant. During the lactation period, the body weights of the dams were decreased.

5.2.3 Dermal application

There are no data available for *n*-decyl oleate.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

In two studies in rabbits, undiluted *n*-decyl oleate was described as very slightly irritating (no other details) (Greim 1998).

After daily dermal application of undiluted *n*-decyl oleate or a 15% aqueous emulsion, two skin samples from each of 3 rabbits were histologically examined after 60 days. Skin irritation occurred at both concentrations (no other details). Undiluted *n*-decyl oleate led to skin thickening in all animals and in one animal to vesicles with congestive dermis. The 15% emulsion caused some papulae or vesicles. The formation of the vesicles was attributed to the formation of an occlusive film on the skin by material that was not completely removed (Guillot et al. 1977).

5.3.2 Eyes

In rabbits, undiluted *n*-decyl oleate was very slightly or not irritating (Greim 1998).

Summary

In rabbits, *n*-decyl oleate is not irritating to the skin and eyes.

5.4 Allergenic effects

5.4.1 Sensitizing effects on the skin

A local lymph node assay (LLNA) carried out according to OECD Test Guideline 429 in female CBA/J mice with 25%, 50% or 100% *n*-decyl oleate in acetone/olive oil (4:1) yielded stimulation indices of 1.17, 1.95 and 2.08, respectively, and thus a clearly negative result (ECHA 2017 a).

The negative result of a maximization test, in which intradermal induction was carried out using 5% preparations of *n*-decyl oleate and topical induction after pretreatment with sodium lauryl sulfate (Greim 1998; Henkel 1979 b, c), cannot be used for the evaluation because the challenge treatment was performed using only 1% preparations.

Also in an earlier study not performed according to test guidelines with intradermal injection of 15% *n*-decyl oleate in 10 guinea pigs, and in a 60-day open patch test using 15% *n*-decyl oleate in addition to undiluted *n*-decyl oleate in groups of 3 rabbits, no evidence of sensitization was found (CIR 1982; Greim 2001). These results are, however, not suitable for inclusion in the evaluation.

5.4.2 Sensitizing effects on the airways

There are no data available.

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

There are no data available for *n*-decyl oleate.

In a study carried out according to OECD Test Guideline 422, groups of 10 male and 10 female Sprague Dawley rats were given gavage doses of **isodecyl oleate** of 0, 100, 300 or 1000 mg/kg body weight and day starting 2 weeks prior to mating. In the males, the daily treatment was carried out for 35 days, in the females up to 3 days after giving birth (see also Section 5.2.2) for a maximum of 56 days. Isodecyl oleate did not cause any substance-related damage to the reproductive organs, spermatogenesis or significant effects on the number of corpora lutea (Zschimmer & Schwarz 2013).

Summary: In Sprague Dawley rats, the NOAEL for the effects of **isodecyl oleate** on fertility is 1000 mg/kg body weight per day, the highest dose tested.

5.5.2 Developmental toxicity

There are no data available for *n*-decyl oleate.

In the study described in Section 5.5.1 and conducted according to OECD Test Guideline 422, male Sprague Dawley rats tolerated **isodecyl oleate** doses of up to 1000 mg/kg body weight and day and females up to 300 mg/kg body weight and day without any substance-related effects. In female animals given isodecyl oleate doses of 1000 mg/kg body weight and day, increased post-implantation losses (21.7%, control animals 7.6%), a 24.4% reduction in total litter weights compared with the value in the control animals and 9 stillbirths (none in the control group) were observed. During the lactation period, the body weights of the dams were reduced by 9.4%. Four days after giving birth, 2 dams had only dead pups: in one case, 3 pups died immediately after birth and 7 were eaten by the mother. In the other case, none of the 11 pups had consumed milk. A total of 30 pups from 3 of the treated dams died, compared with 5 pups from 10 control animals. Only in the 3 animals with dead pups was the feed intake reduced (by 42% to 72%). The authors considered the complete loss of offspring in 2 of 7 dams to be substance-related (Zschimmer & Schwarz 2013).

Summary: For the structural analogue **isodecyl oleate**, the NOAEL for developmental toxicity in Sprague Dawley rats is 300 mg/kg body weight and day. At 1000 mg/kg body weight and day, the incidences of post-implantation losses, stillbirths and not viable offspring were increased. During the lactation period, body weight losses were observed in the dams. Similar effects are expected for *n*-decyl oleate.

5.6 Genotoxicity

5.6.1 In vitro

n-Decyl oleate was not mutagenic in Salmonella mutagenicity tests with the Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations up to 2500 µg/plate in the presence and in the absence of a metabolic activation system (Henkel 1979 a). Studies with structural analogues, such as **2-octyldodecyl isooctadecanoate**, **2-ethylhexyl oleate**, **oleyl oleate** or **C16-18 fatty acid isotridecyl ester** likewise did not yield genotoxic effects in bacteria or mammalian cells (see Table 2) (ECHA 2017 b).

Tab. 2 Genotoxicity of n-decyl oleate and structural analogues in vitro

End point	Test system	Concentration [µg/plate][a)]	Effective concentration[a)]	Cytotoxicity[a)]	Result		References
					–m. a.	+m. a.	
***n*-Decyl oleate**							
gene mutation	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	4–2500	–	–	–	–	Henkel 1979 a

Tab. 2 *(continued)*

End point	Test system	Concentration [µg/plate][a)]	Effective concentration[a)]	Cytotoxicity[a)]	Result		References
					–m. a.	+m. a.	
2-Octyldodecyl isooctadecanoate							
gene mutation	Salmonella typhimurium TA98, TA100, TA1535, TA1537, Escherichia coli WP2 uvr A	0, 10, 33, 100, 333, 1000	–	–	–	–	ECHA 2017 b
CA	human lymphocytes	0, 333, 1000 µg/ml	–	–	–	–	ECHA 2017 b
2-Ethylhexyl oleate (purity > 60%)							
CA	human lymphocytes	0, 3, 10, 33 µg/ml	–	33 µg/ml precipitation	–	–	ECHA 2017 b
gene mutation $TK^{+/-}$	mouse lymphoma L5178Y cells	0.03, 0.1, 0.3, 1, 3, 10, 33, 100 µg/ml	–	≥ 333 µg/ml precipitation	–	–	ECHA 2017 b
Oleyl oleate							
CA	V79 cells	0, 10, 60, 100 µg/ml	–	> 100 µg/ml precipitation	–	–	ECHA 2017 b
gene mutation HPRT	V79 cells	10, 30, 60, 100 µg/ml	–	> 100 µg/ml precipitation	–	–	ECHA 2017 b
C16–18 fatty acid isotridecyl ester							
gene mutation	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	8, 40, 200, 1000, 5000	–	–	–	–	ECHA 2017 b

[a)] Values are given in µg/plate unless otherwise indicated
CA: chromosomal aberration; HPRT: hypoxanthine phosphoribosyl transferase locus; –m. a.: without metabolic activation; +m. a.: with metabolic activation; TK: thymidine kinase locus

5.6.2 In vivo

There are no in vivo data available for *n*-decyl oleate.

Groups of 5 male and 5 female Swiss CD1 mice were given single intraperitoneal injections of **2-octyldodecyl isooctadecanoate** (in corn oil) of 0, 500, 1000 or 2000 mg/kg body weight. Examination of the bone marrow cells after 24 or 48 hours did not reveal an increase in the incidence of micronuclei. The ratio between polychromatic and normochromatic cells was not significantly altered (ECHA 2017 b).

Conclusion: *n*-Decyl oleate was not mutagenic in Salmonella mutagenicity tests. Since investigations with the structural analogues **2-ethylhexyl oleate** or **oleyl oleate** did not yield genotoxic effects in mammalian cells and **2-octyldodecyl isooctadecanoate** did not induce micronuclei in the bone marrow of mice, it can be assumed that also *n*-decyl oleate is not genotoxic in these test systems.

5.7 Carcinogenicity

There are no data available for *n*-decyl oleate.

6 Manifesto (MAK value/classification)

The critical effect is the assumed accumulation of *n*-decyl oleate in the lungs due to its poor solubility in water.

MAK value. Data from humans suitable for an evaluation or inhalation studies with *n*-decyl oleate in rats or mice are not available.

However, there is a study with the structural analogue **isodecyl oleate** carried out according to OECD Test Guideline 422. This study in Sprague Dawley rats given daily gavage doses of **isodecyl oleate** of up to 1000 mg/kg body weight and day 2 weeks prior to mating up to 3 days after giving birth for a maximum of 56 days, yielded a NOAEL of 300 mg/kg body weight and day based on body weight losses in the dams. The following toxicokinetic data are taken into consideration for the extrapolation of this NOAEL to a concentration in workplace air: the species-specific toxicokinetic correction value for the rat (1:4), the body weight and respiratory volume (10 m^3) of the person (70 kg), the assumed 100% inhalation and oral absorption and the daily exposure of the animals in comparison with the 5 days per week exposure at the workplace (7:5). The concentration calculated from this is 735 mg isodecyl oleate/m^3. Applying the factor 2 for the possible increase in effects over time and for the extrapolation of data from animal experiments to humans, and using the "preferred value approach", a MAK value of 100 mg **isodecyl oleate**/m^3 I (inhalable fraction) would be obtained due to the systemic toxicity in the dams, which could also apply for *n*-decyl oleate by analogy. However, this value cannot be used for inhalation exposure because as soon as *n*-decyl oleate is inhaled, it most likely accumulates in the lungs due to its poor solubility in water, as is the case with pharmaceutical white mineral oil. Because of the expected lung toxicity, a MAK value of 5 mg/m^3 R (respirable fraction) has been established for *n*-decyl oleate in analogy to that for pharmaceutical white mineral oil.

Peak limitation. In analogy to pharmaceutical white mineral oil, which, due to its cumulative, late-onset effect is assigned to Peak Limitation Category II with an excursion factor of 4, *n*-decyl oleate has likewise been assigned to Peak Limitation Category II with an excursion factor of 4.

Absorption through the skin. Quantitative data for the absorption of the substance through the skin are not available. Model calculations are not permitted due to its extremely poor solubility in water and especially due to the extremely high log K_{OW}. *n*-Decyl oleate did not cause systemic effects in Wistar rats in acute toxicity studies after dermal application up to the highest dose tested (2000 mg/kg body weight). *n*-Decyl oleate is therefore not designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. There are not sufficient clinical findings of skin sensitization caused by *n*-decyl oleate in humans. Experimental studies have provided no evidence of contact sensitization, and a valid local lymph node assay in mice yielded a negative result. There are no findings of respiratory sensitization. *n*-Decyl oleate is therefore not designated with "Sh" or "Sa" (for substances which cause sensitization of the skin or airways).

Prenatal toxicity. Because there are no studies with *n*-decyl oleate, the study carried out according to OECD Test Guideline 422 in rats is used, in which the structural analogue **isodecyl oleate** was administered for a maximum of 56 days. The gavage administration of **isodecyl oleate**, starting 2 weeks prior to mating up to 3 days after giving birth, yielded a NOAEL of 300 mg/kg body weight and day, based on maternal and pronounced developmental toxicity. After toxicokinetic extrapolation (see above) this value corresponds to a concentration in workplace air of 735 mg/m^3. There are no studies of teratogenicity. Since the available data are not sufficient for a final evaluation, **isodecyl oleate** is assigned to Pregnancy Risk Group D. In analogy to **isodecyl oleate**, *n*-decyl oleate has also been assigned to Pregnancy Risk Group D.

Carcinogenicity and germ cell mutagenicity. *n*-Decyl oleate is not mutagenic in bacteria. There are no studies of carcinogenicity and genotoxicity in animal experiments. Since studies with the structural analogues **2-octyldodecyl isooctadecanoate**, **2-ethylhexyloleate**, **oleyl oleate** or **C16-18 fatty acid isotridecyl ester** did not reveal genotoxic effects in bacteria or mammalian cells, it can be assumed that also *n*-decyl oleate is not genotoxic in these test systems. Therefore, the substance is not classified in one of the categories for carcinogens or germ cell mutagens.

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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