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2-Ethylhexyl oleate

MAK Value Documentation – Translation of the German version from 2022

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Keywords

2-ethylhexyl oleate; lung toxicity; overload; inflammation; microgranuloma; MAK value; maximum workplace concentration; aerosol; developmental toxicity; read-across

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-ethylhexyl oleate [26399-02-0] to derive an occupational exposure limit value (maximum concentration at the workplace, MAK value), considering all toxicological end points. Available publications are described in detail. As with white mineral oil, inhalation of aerosols of the hardly water-soluble 2-ethylhexyl oleate could result in overload in the lung, inflammatory reactions and microgranulomas. To prevent this overload, a MAK value of 5 mg/m^3 for the respirable fraction is established by analogy with white mineral oil and Peak Limitation Category II as well as an excursion factor of 4 is set. The substance is classified in Pregnancy Risk Group D because developmental toxicity studies are lacking. 2-Ethylhexyl oleate is not genotoxic. Carcinogenicity studies are not available. There are no indications of a sensitizing potential of 2-ethylhexyl oleate. Skin contact is not expected to contribute significantly to systemic toxicity.

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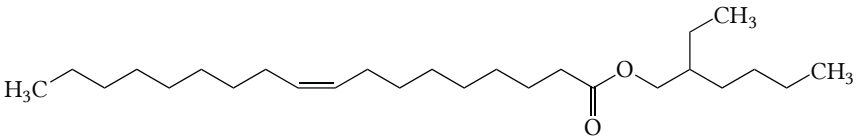
MAK value (2021)	**5 mg/m³ R (respirable fraction)**
Peak limitation (2021)	**Category II, excursion factor 4**
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2021)	**Pregnancy Risk Group D**
Germ cell mutagenicity	–
BAT value	–
Synonyms	2-ethylhexyl-9-octadecenoate 2-ethylhexanol oleic acid ester 9-octadecenoic acid (9Z)-2-ethylhexyl ester oleic acid 2-ethylhexyl ester
Chemical name	2-ethylhexyl (Z)-octadec-9-enoate
CAS number	26399-02-0
Structural formula	
Molecular formula	$C_{26}H_{50}O_2$
Molar mass	394.7 g/mol
Melting point	< −20 °C (IFA 2020), −20 °C (ECHA 2020)
Boiling point	> 300 °C, decomposition possible (ECHA 2020)
Density	0.87 g/cm³ (ECHA 2020; IFA 2020)
Vapour pressure	0.000024 hPa (ECHA 2020)
log K_{OW}	10.7 (calculated) (NCBI 2021), > 10 (calculated) (ECHA 2020)
Solubility	< 1 mg/l water (ECHA 2020)
1 ml/m³ (ppm) ≙ 16.38 mg/m³	**1 mg/m³ ≙ 0.0611 ml/m³ (ppm)**
Hydrolytic stability	no data
Stability	no data
Production	esterification of oleic acid with 2-ethylhexanol (Lacaze-Dufaure and Mouloungui 2000; da Silva et al. 2020)
Purity	no data
Impurities	possibly oleic acid and 2-ethylhexanol
Uses	in adhesives and sealants, dyes, functional fluids (open systems), lubricants and lubricant additives, processing aid specific to petroleum production, solvents (for cleaning and degreasing), detergents and care products, in dyes and coatings (NCBI 2021), in formulations of creams, lotions and other cosmetics to maintain skin hydration and plasticity, use as an emollient (softening properties) in cosmetics (da Silva et al. 2020)

Concentrations used	contained in metal-working fluid concentrate up to a maximum fraction (w/w) of 20% (Hartwig and MAK Commission 2018, available in German only), no data for concentrations used

After the hydrolysis of 2-ethylhexyl oleate or during its metabolism, the corresponding alcohol and the corresponding fatty acid, namely 2-ethylhexanol and oleic acid, are formed (Section 3.2; Greim 2002, 2003). Therefore, also data for the metabolites are given in some cases.

For the evaluation of 2-ethylhexyl oleate, also data listed in the REACH registration dossier for the class of "short chain alcohol esters" are used. Included here are esters of a fatty acid (C8 to C29) and a C2 to C8 alcohol (ethanol, 2-propanol, 1-butanol, 2-butanol, pentanol, 2-pentanol, 1-hexanol, 2-ethylhexanol or 1-octanol). The class includes both defined mono-constituted substances and related UVCB substances (substances of Unknown or Variable composition, Complex reaction products or Biological materials) with varying fatty acid chain lengths (ECHA 2018).

2-Ethylhexyl oleate is an oily liquid (IFA 2020) with a very low water solubility of less than 1 mg/l water (ECHA 2020). The viscosity is 7.8 cSt at 40 °C (ECHA 2020), which means the substance has a low viscosity (thin). A viscosity of more than 3 cSt at 40 °C is given for white mineral oil (ECHA 2021).

Two further esters with an oleate residue, *n*-decyl oleate and isodecyl oleate, were both assumed to be analogous to white mineral oil (Hartwig and MAK Commission 2021 a, b).

1 Toxic Effects and Mode of Action

Exposure to the aerosol of 2-ethylhexyl oleate, by analogy with white mineral oil, is likely to result in macrophage accumulation and the formation of microgranulomas in the lungs. However, inhalation studies are not available.

Hydrolysis of the fatty acid ester 2-ethylhexyl oleate produces oleic acid and the corresponding alcohol 2-ethylhexanol. Data for the 2 metabolites 2-ethylhexanol and oleic acid are available for rats. Systemic toxicity in the form of liver dysfunction and peroxisome proliferation in the liver was observed after gavage doses of 2-ethylhexanol of 250 mg/kg body weight and day and above for 13 weeks. Systemic toxicity is less pronounced after treatment with oleic acid; underdeveloped mammary glands and, in some cases, ovarian cysts were observed at about 7500 mg/kg body weight and day after administration with the diet for 10 to 16 weeks.

2-Ethylhexyl oleate is not irritating to the skin and eyes of rabbits.

No findings in humans and no studies in animals are available for skin sensitizing effects of 2-ethylhexyl oleate. There are also no data available for respiratory sensitization caused by 2-ethylhexyl oleate.

Studies of reproductive toxicity have not been performed with 2-ethylhexyl oleate. There is no evidence of reproductive toxicity or teratogenicity for the 2 metabolites 2-ethylhexanol and oleic acid.

2-Ethylhexyl oleate was not found to have genotoxic potential.

Carcinogenicity studies are not available. The metabolites 2-ethylhexanol and oleic acid are not regarded as carcinogenic to humans.

2 Mechanism of Action

Fatty acid esters are hydrolysable in the organism. Hydrolysis by lipases leads to cleavage of the ester bond, resulting in the corresponding fatty acid and alcohol; in the case of 2-ethylhexyl oleate, these are oleic acid and 2-ethylhexanol.

Lipases are found also in the lungs, mainly in the alveolar macrophages; this is described in detail in the MAK documentation for triglycerides (Hartwig and MAK Commission 2024)

Inhaled mineral oil is known to accumulate in the lungs and, due to incomplete phagocytosis by alveolar macrophages, causes inflammatory reactions (exogenous lipid pneumonia), microgranulomas and even fibrotic changes (Eckert and Jerochin 1981; SCOEL 2011).

Mechanistically, the changes in the lungs caused by mineral oil can be explained by an overload effect as a result of the accumulation of the oil in alveolar macrophages (Hartwig and MAK Commission 2019). Mineral oil, as a mixture of predominantly saturated hydrocarbons, is not hydrolysable because it does not contain any hydrocarbons with ester bonds.

Fatty acid esters taken up by inhalation in aerosol form can likewise be assumed to accumulate in the alveolar macrophages. However, they can be degraded there by lipases. Only if the hydrolysis capacity of the lipases is exceeded can overloading occur with the corresponding consequential effects. Unlike for mineral oil, however, it is unclear at what concentration of fatty acid esters an overload effect is to be expected.

Analogy to white mineral oil/mineral oil is used to represent a worst case scenario, as explained in Section 6.

The effects of oleic acid after intravenous and intratracheal administration are discussed in detail in the MAK documentation for *n*-decyl oleate and isodecyl oleate (Hartwig and MAK Commission 2021 a, b).

3 Toxicokinetics and Metabolism

3.1 Absorption, distribution, elimination

Studies with 2-ethylhexyl oleate have not been carried out.

Due to its low vapour pressure, 2-ethylhexyl oleate is more likely to occur as an aerosol than as vapour (ECHA 2020; IFA 2020). Systemic bioavailability is considered probable after inhalation of the substance (ECHA 2018).

After oral uptake, systemic bioavailability of 2-ethylhexyl oleate and its metabolites is to be expected (ECHA 2020).

Studies of the absorption of 2-ethylhexyl oleate through the skin are not available. Due to the physicochemical properties of the substance (low water solubility, high molar mass and, in particular, a high log K_{OW} value), model calculations are not possible. For structurally analogous oleic acid esters with similar molar masses, such as *n*-decyl oleate or isodecyl oleate, dermal absorption to any relevant extent is not assumed (Hartwig and MAK Commission 2021 a, b). Skin irritating properties of the substance would be an indication of the ability of 2-ethylhexyl oleate to penetrate the skin. However, no evidence of a significant skin irritation potential was found.

For 2-ethylhexyl oleate, the main route of excretion is expected to be by expired air as CO_2 after metabolic degradation (ECHA 2020).

3.2 Metabolism

Metabolism studies with 2-ethylhexyl oleate are not available.

Fatty acid esters are hydrolysed via esterases to the corresponding alcohol and fatty acid; 2-ethylhexyl oleate leads to 2-ethylhexanol and oleic acid (ECHA 2020; IFA 2020). In the case of 2-ethylhexanol, oxidative conversion to 2-ethylhexanoic acid and the subsequent formation of metabolites is expected. Excretion occurs mainly in the form of the glucuronide with the urine (IFA 2020). As with all fatty acids, oleic acid is degraded by successive β-oxidation and cleavage of the terminal C_2 unit as the acetyl thioester of coenzyme A (Greim 2002).

4 Effects in Humans

Studies in humans following exposure to 2-ethylhexanol are not available. Also for the structurally closely related substances isodecyl oleate and *n*-decyl oleate, there are no or no valid reports of allergic reactions (Hartwig and MAK Commission 2021 a, b).

5 Animal Experiments and in vitro Studies

5.1 Acute toxicity

5.1.1 Inhalation

2-Ethylhexyl oleate was investigated in a study carried out according to OECD Test Guideline 436 in 3 male and 3 female Crl:WI (Han) rats per concentration group. For this purpose, the animals were exposed nose-only for 4 hours to an aerosol concentration of 5700 mg/m^3 (mass median aerodynamic diameter 2.5 µm). All animals displayed hunched posture on the second day after exposure. There were no further clinical signs and no effects on body weights or mortality within the 14-day observation period. Gross pathological examination did not reveal any unusual findings. The 4-hour LC_{50} was thus more than 5700 mg/m^3 (ECHA 2020; IFA 2020).

From the class of short-chain alcohol esters, 3 substances were tested. Their 4-hour LC_{50} values exceeded 5000 mg/m^3 (ECHA 2018).

5.1.2 Oral administration

Five female NMRI-EOPS mice were given a single gavage dose of 2-ethylhexyl oleate of 5000 mg/kg body weight. The animals were observed for 6 days, necropsy was not performed. There were no deaths or adverse clinical signs. The LD_{50} is therefore greater than 5000 mg/kg body weight (ECHA 2020; IFA 2020).

5.1.3 Dermal application

There are no data available for 2-ethylhexyl oleate.

From the class of short-chain alcohol esters, 2 substances were tested for which dermal LD_{50} values of more than 2000 mg/kg body weight were obtained (ECHA 2018).

5.2 Subacute, subchronic and chronic toxicity

5.2.1 Inhalation

There are no data available.

5.2.2 Oral administration

No studies have been carried out with 2-ethylhexyl oleate.

Data are available for the 2 metabolites. 2-Ethylhexanol caused liver dysfunction and peroxisome proliferation in the liver at 250 mg/kg body weight and day and above in a 13-week gavage study in rats. The NOAEL was 125 mg/kg body weight and day (Greim 2003).

In a feeding study with oleic acid for 10 to 16 weeks, underdeveloped mammary glands and, in some animals, ovarian cysts were observed in female rats at about 7500 mg/kg body weight and day (Greim 2002).

Studies in rats with subacute and subchronic administration of various substances from the class of short-chain alcohol esters yielded NOAELs of 1000 mg/kg body weight and day and above (ECHA 2018, 2020).

5.2.3 Dermal application

There are no data available.

5.3 Local effects on skin and mucous membranes

5.3.1 Skin

In a study carried out according to OECD Test Guideline 404, 0.5 ml of undiluted 2-ethylhexyl oleate (purity not specified) was applied occlusively for 4 hours to 3 New Zealand White rabbits. The animals were examined 1, 24, 48 and 72 hours after application. After 1 hour, slight redness was found in 1 animal, and well-defined erythema was noted in a second animal (grade 1 and 2, respectively, on a scale with a maximum of 4; individual index at 24, 48 and 72 hours: 0.33, 0, 0.33). Very slight and slight oedema, respectively, were observed in 2 animals after 1 hour (grade 1 and 2, respectively, on a scale with a maximum of 4; individual index at 24, 48 and 72 hours: 0.33, 0, 0). All effects were completely reversible within 48 hours in all animals. The substance was regarded as not irritating to the skin (ECHA 2020; IFA 2020).

While in some studies with short-chain alcohol esters no skin irritation was found in the rabbit, other studies demonstrated a slight skin irritating potency (ECHA 2018).

5.3.2 Eyes

Fatty acid esters similar to 2-ethylhexyl oleate, for example the shorter-chain ethylhexyl laurate, did not cause significant eye irritation in rabbits in valid tests (IFA 2020).

Several studies with short-chain alcohol esters were performed in rabbits. None of the studies revealed an eye irritation potential (ECHA 2018).

5.4 Allergenic effects

There are no studies with 2-ethylhexyl oleate. A valid local lymph node assay with the structurally closely related *n*-decyl oleate yielded an unequivocally negative result (Hartwig and MAK Commission 2021 b).

5.5 Reproductive and developmental toxicity

5.5.1 Fertility

There are no data available for 2-ethylhexyl oleate.

Fertility was not impaired in studies with the 2 metabolites 2-ethylhexanol and oleic acid (Greim 2002, 2003).

Reproductive toxicity studies were conducted with 2 short-chain alcohol esters. The NOAELs for fertility were 5500 and 6000 mg/kg body weight and day, respectively, the highest doses tested in each case (ECHA 2018).

5.5.2 Developmental toxicity

No studies have been carried out with 2-ethylhexyl oleate.

The metabolite 2-ethylhexanol was not teratogenic in rats (Greim 2003). There are no valid developmental toxicity studies for the metabolite oleic acid (Hartwig and MAK Commission 2017 a).

Two short-chain alcohol esters were investigated in prenatal developmental toxicity studies. Teratogenic effects were not observed. The NOAELs for developmental and maternal toxicity were 1000 mg/kg body weight and day, the highest dose tested in each case (ECHA 2018).

5.6 Genotoxicity

5.6.1 In vitro

In a chromosomal aberration test carried out according to OECD Test Guideline 473 in human peripheral lymphocytes with 2-ethylhexyl oleate concentrations of 3, 10 or 33 µg/ml (purity of the test substance not specified, solvent: ethanol) with and without the addition of a metabolic activation system, no clastogenic effects occurred. No cytotoxicity was observed up to the highest concentration tested. At 33 µg/ml precipitation of the test substance occurred (ECHA 2020).

In a $TK^{+/-}$ mutation assay with L5178Y mouse lymphoma cells carried out according to OECD test guideline 476, 2-ethylhexyl oleate was tested at concentrations of 0.03, 0.1, 0.3, 1.0, 3.0, 10, 33 and 100 µg/ml with and without the addition of a metabolic activation system (purity of the test substance not specified, solvent: ethanol). The test substance was not mutagenic. Cytotoxicity did not occur up to the highest concentration tested. At 100 µg/ml precipitation of the test substance was observed (ECHA 2020; IFA 2020).

The metabolite 2-ethylhexanol was not genotoxic in vitro (Greim 2003).

The metabolite oleic acid was not mutagenic in bacteria, but caused increased mitotic aneuploidy in yeast and mammalian cells (Greim 2002).

In a large number of in vitro tests carried out according to valid test guidelines, mutagenic or clastogenic effects of short-chain alcohol esters were not observed (ECHA 2018).

5.6.2 In vivo

There are no data available.

5.7 Carcinogenicity

There are no data available for 2-ethylhexyl oleate.

The metabolites 2-ethylhexanol and oleic acid are not carcinogenic (Greim 2003; Hartwig and MAK Commission 2017 a).

There is no evidence of carcinogenic effects of short-chain alcohol esters (ECHA 2018).

6 Manifesto (MAK value/classification)

The critical effect is the assumed accumulation of 2-ethylhexyl oleate in the lungs due to its low water solubility. Because of its low vapour pressure, exposure to the substance is to be expected only in aerosol form but not as vapour. As with white mineral oil, this could lead to macrophage accumulation and the formation of microgranulomas in the lungs.

MAK value. There are no human data or inhalation studies in animals with 2-ethylhexyl oleate suitable for inclusion in the evaluation.

In the case of mineral oils such as white mineral oil, an overload effect in the lungs occurs when concentrations are too high (Hartwig and MAK Commission 2017 b). Whereas mineral oils are not hydrolysable, fatty acid esters such as 2-ethylhexyl oleate can undergo hydrolysis. Therefore, if the hydrolysis capacity is exceeded, overloading in the lungs may likewise occur. The limit of the hydrolysis capacity is not known; it is thus unclear at which concentration an

overload effect is to be expected. Therefore, it is assumed as a worst case scenario that overloading of the lungs occurs at the same concentration as that for white mineral oil.

A MAK value of 5 mg/m^3 R (respirable fraction) has therefore been established for 2-ethylhexyl oleate, in analogy to that for white mineral oil. This concentration will probably not be reached when used in metal-working fluids if the corresponding technically based limit value of 10 mg/m^3 I (inhalable fraction) is observed.

No data are available for the systemic toxicity of 2-ethylhexyl oleate. Of the possible metabolites, oleic acid caused underdeveloped mammary glands and, in some cases, ovarian cysts only at a dose level of 7500 mg/kg body weight and day (Greim 2002). In contrast, 2-ethylhexanol resulted in liver dysfunction and peroxisome proliferation in the liver in a 13-week gavage study with rats at 250 mg/kg body weight and day. The NOAEL is 125 mg/kg body weight and day (Greim 2003). The following toxicokinetic data are taken into consideration for the extrapolation of this NOAEL of 125 mg 2-ethylhexanol/kg body weight and day in the rat to a concentration in workplace air: the species-specific toxicokinetic correction value (1:4) for the rat, the assumed oral absorption (100%), the body weight (70 kg) and the respiratory volume (10 m^3) of the person, and the assumed 100% absorption by inhalation. The concentration calculated from this is 219 mg 2-ethylhexanol/m^3. Taking the molar mass (2-ethylhexanol is about ¼ of the molar mass of 2-ethylhexyl oleate) into account, this is far above the MAK value of 5 mg 2-ethylhexyl oleate/m^3 R. Even if exposure to the I fraction were far higher than that to the R fraction, systemic effects due to the metabolite 2-ethylhexanol are not to be assumed.

The following data are available for local effects of the metabolites:

In rabbits, 2-ethylhexanol has an irritant to strongly irritant effect on the skin and eyes (Greim 2003) and, due to the irritant effect on the eyes observed in a study in volunteers, has been assigned a MAK value of 10 ml/m^3 (54 mg/m^3) (Hartwig 2012, available in German only). By contrast, 2-ethylhexyl oleate is hardly irritating at all. In view of the lower MAK value for 2-ethylhexyl oleate of 5 mg/m^3, irritant effects in the lungs from 2-ethylhexanol are therefore not to be expected.

Oleic acid is not or only very slightly irritating to the rabbit eye (Greim 2002; Hartwig and MAK Commission 2017 a), therefore a local irritant effect in the lungs from the oleic acid released during hydrolysis is not to be expected. Furthermore, plant and animal triglycerides, which can likewise be assumed to be hydrolysed in the lungs to glycerol and the corresponding long-chain alkyl acids, lead to effects in the lungs similar to those caused by mineral oil, but they are less pronounced (Hartwig and MAK Commission 2024). Therefore, local effects due to the metabolite oleic acid are likewise covered by the MAK value for 2-ethylhexyl oleate.

Peak limitation. The effects in the lungs constitute a cumulative, late-onset effect (Hartwig and MAK Commission 2017 b); the substance has therefore been assigned to Peak Limitation Category II. In analogy to pharmaceutical white mineral oil and polyalphaolefins, 2-ethylhexyl oleate has been given an excursion factor of 4, since very high peak concentrations could possibly change the distribution behaviour in the alveoli, and thus also the retention period; at all times, the formation of microgranulomas in the lungs must be prevented (Hartwig 2011, available in German only).

Prenatal toxicity. Developmental toxicity studies according to valid test guidelines are not available for 2-ethylhexyl oleate. Therefore, the substance has been assigned to Pregnancy Risk Group D.

Carcinogenicity. No carcinogenicity studies have been carried out with 2-ethylhexyl oleate.

The metabolites 2-ethylhexanol and oleic acid are not carcinogenic and are not classified in one of the categories for carcinogens (Greim 2003; Hartwig and MAK Commission 2017 a).

In view of its structure, 2-ethylhexyl oleate is not suspected of causing carcinogenic effects. The substance has not been classified in one of the categories for carcinogens.

Germ cell mutagenicity. 2-Ethylhexyl oleate is not mutagenic or clastogenic in mammalian cells in vitro (ECHA 2020; IFA 2020). The metabolite 2-ethylhexanol has been shown not to be genotoxic in vitro (Greim 2003). The metabolite oleic acid is not mutagenic in bacteria, but increased mitotic aneuploidy in yeast and mammalian cells. The substance

has not been classified in one of the categories for germ cell mutagens (Greim 2002; Hartwig and MAK Commission 2017 a). A large number of in vitro tests carried out according to valid test guidelines did not reveal any mutagenic or clastogenic effects for short-chain alcohol esters (ECHA 2018). Thus, in view of the structure of 2-ethylhexyl oleate, genotoxic effects are not suspected. Therefore, 2-ethylhexyl oleate has not been classified in one of the categories for germ cell mutagens.

Absorption through the skin. Quantitative data for the absorption of 2-ethylhexyl oleate through the skin are not available. Model calculations are not possible due to the extremely low water solubility and, in particular, due to the high log K_{OW}. Studies of the potential of 2-ethylhexyl oleate to cause irritation do not indicate that the substance is absorbed through the skin to any significant degree. For the structurally related oleic acid esters with a similar molar mass, animal tests after single or repeated dermal application provided no evidence of systemic toxicity by dermal absorption up to the respective highest doses tested (2000 and 1000 mg/kg body weight and day). Therefore, 2-ethylhexyl oleate has not been designated with an "H" (for substances which can be absorbed through the skin in toxicologically relevant amounts).

Sensitization. Findings in humans and experimental studies in animals or in vitro are not available for the sensitizing effects of 2-ethylhexyl oleate on the skin and airways. A valid local lymph node assay in mice with the structurally very similar *n*-decyl oleate yielded a negative result. 2-Ethylhexyl oleate has therefore not been designated with "Sh" or "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.

References

ECHA (European Chemicals Agency) (2018) Isopropyl oleate (CAS Number 112-11-8). Registration dossier. Joint submission, first publication 25 Jun 2013, last modification 03 Sep 2018. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/13373, accessed 23 Oct 2020

ECHA (European Chemicals Agency) (2020) 2-Ethylhexyl oleate (CAS Number 26399-02-0). Registration dossier. Joint submission, first publication 03 Mar 2011, last modification 09 Mar 2020. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15935, accessed 21 Apr 2020

ECHA (European Chemicals Agency) (2021) White mineral oil (petroleum) (CAS Number 8042-47-5). Registration dossier. Joint submission, first publication 16 Mar 2011, last modification 01 Mar 2021. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15514, accessed 12 Apr 2021

Eckert H, Jerochin S (1981) Die Pathogenese der sogenannten exogenen Lipoidpneumonie. Z Erkr Atmungsorgane 157(1): 27–33

Greim H, editor (2002) Oleic acid. MAK Value Documentation, 1998. In: Occupational Toxicants. Volume 17. Weinheim: Wiley-VCH. p. 245–266. Also available from https://doi.org/10.1002/3527600418.mb11280kske0017

Greim H, editor (2003) 2-Ethylhexanol. MAK Value Documentation, 2000. In: Occupational Toxicants. Volume 20. Weinheim: Wiley-VCH. p. 135–178. Also available from https://doi.org/10.1002/3527600418.mb10476kske0020

Hartwig A, editor (2011) Polyalphaolefine. In: Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründung von MAK-Werten. 51st issue. Weinheim: Wiley-VCH. Also available from https://doi.org/10.1002/3527600418.mb6864911d0051

Hartwig A, editor (2012) 2-Ethylhexanol. In: Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründung von MAK-Werten. 53rd issue. Weinheim: Wiley-VCH. Also available from https://doi.org/10.1002/3527600418.mb10476kskd0053

Hartwig A, MAK Commission (2017 a) Oleic acid. MAK Value Documentation, 2016. MAK Collect Occup Health Saf 1(2): 455–460. https://doi.org/10.1002/3527600418.mb11280kske6017

Hartwig A, MAK Commission (2017 b) White mineral oil, pharmaceutical. MAK Value Documentation, 2015. MAK Collect Occup Health Saf 2(3): 1177–1191. https://doi.org/https://doi.org/10.1002/3527600418.mb804247kske5917

Hartwig A, MAK Commission (2018) Komponenten von Kühlschmierstoffen, Hydraulikflüssigkeiten und anderen Schmierstoffen. MAK Value Documentation in German language. MAK Collect Occup Health Saf 3(3): 1417–1471. https://doi.org/10.1002/3527600418.mb0215khsd0065

Hartwig A, MAK Commission (2019) Mineral oils (petroleum), severely refined. MAK Value Documentation, 2018. MAK Collect Occup Health Saf 4(1): 36–50. https://doi.org/10.1002/3527600418.mb9206235e6519

Hartwig A, MAK Commission (2021 a) Isodecyl oleate. MAK Value Documentation, supplement – Translation of the German version from 2019. MAK Collect Occup Health Saf 6(3): Doc059. https://doi.org/10.1002/3527600418.mb5923134kske6_3ad

Hartwig A, MAK Commission (2021 b) n-Decyl oleate. MAK Value Documentation, supplement – Translation of the German version from 2019. MAK Collect Occup Health Saf 6(3): Doc056. https://doi.org/10.1002/3527600418.mb368746kske6_3ad

Hartwig A, MAK Commission (2024) Triglycerides (lard oil, palm oil, rapeseed oil, soybean oil). MAK Value Documentation – Translation of the German version from 2022. MAK Collect Occup Health Saf 9(2): Doc37. https://doi.org/10.34865/mbtriglykske9_2or

IFA (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) (2020) 2-Ethylhexyloleat. GESTIS-Stoffdatenbank. https://gestis.dguv.de/data?name=135733, accessed 17 Apr 2020

Lacaze-Dufaure C, Mouloungui Z (2000) Catalysed or uncatalysed esterification reaction of oleic acid with 2-ethyl hexanol. Appl Catal A Gen 204(2): 223–227. https://doi.org/10.1016/S0926-860X(00)00533-0

NCBI (National Center for Biotechnology Information) (2021) 2-Ethylhexyl oleate. PubChem compound summary for CID 6438028. https://pubchem.ncbi.nlm.nih.gov/compound/6438028, accessed 19 Mar 2021

SCOEL (Scientific Committee on Occupational Exposure Limits) (2011) Recommendation from the Scientific Committee on Occupational Exposure Limits for aerosols of severely refined mineral oils. SCOEL/SUM/163. Brussels: European Commission

da Silva MVC, Rangel ABS, Aguiar LG, de Castro HF, de Freitas L (2020) Continuous enzymatic synthesis of 2-ethylhexyl oleate in a fluidized bed reactor: operating conditions, hydrodynamics, and mathematical modeling. Ind Eng Chem Res 59(44): 19522–19530. https://doi.org/10.1021/acs.iecr.0c03504