GreenScreen® Chemical Assessment

1-Tetradecanol *(CAS# 112-72-1)*

Method Version: GreenScreen® Version 1.4

Assessment Details:

Assessment Type:	Certified
Assessment Prepared By:	WAP Sustainability Consulting, LLC (Eric Rosenblum Ph.D. DABT and Donald K. Ward, NSF International)
Assessment Prepared For:	Public Benefit
Date Assessment Completed:	May 13th, 2019
Assessment Expiration Date:	May 13th, 2024
Assessor Type:	Licensed GreenScreen® Profiler

1701 Market St., Chattanooga, TN 37421
info@wapsustainability.com • 855.452.2522

GREENSCREEN BENCHMARK™ SUMMARY:

This chemical assessment report includes a GreenScreen Benchmark™ score and results for Tetradecanol (CASRN 112-72-1) only.

No marketing claims can be made without licensing through Clean Production Action.

GreenScreen Benchmark Score:
Tetradecanol was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has Very High chronic aquatic toxicity (CA). This corresponds to GreenScreen® benchmark classification 2f in CPA 2018. Data gaps (DG) exist for endocrine activity (E), repeat dose neurotoxicity (N), and respiratory sensitization (SnR). As outlined in CPA (2018) Section I 11.6.2 (Step b – Determine the final Benchmark score), Tetradecanol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if Tetradecanol were assigned a High score for data gap endocrine activity it would be categorized as a Benchmark 1 Chemical.

HAZARD CLASSIFICATION SUMMARY

Table 1. GreenScreen Hazard Summary Table:[1]

GreenScreen Hazard Summary Table for Tetradecanol																			
Group I Human					**Group II and II* Human**										**Ecotox**		**Fate**		**Physical**	
Carcinogenicity	**Genotoxicity/Mutagenicity**	**Reproductive Toxicity**	**Developmental Toxicity**	**Endocrine Activity**	**Acute Toxicity**	**Systemic Toxicity**		**Neurotoxicity**		**Skin Sensitization***	**Respiratory Sensitization***	**Skin Irritation**	**Eye Irritation**		**Acute Aquatic Toxicity**	**Chronic Aquatic Toxicity**	**Persistence**	**Bioaccumulation**	**Reactivity**	**Flammability**
						single	repeat*	single	repeat*	*	*									
L	**L**	**L**	**L**	DG	**L**	**L**	**L**	*M*	DG	**L**	DG	**H**	**M**		*H*	**vH**	**vL**	*M*	*L*	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that Group II Human Health endpoints have four hazard scores (i.e., vH, H, M and L) instead of three (i.e., H, M and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints.

[1] See Appendix A for a glossary of hazard endpoint acronyms.

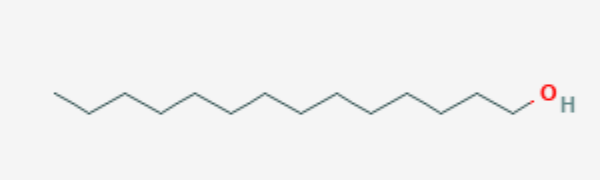
SCOPE OF ASSESSMENT

1-Tetradecanol (CASRN 112-72-1):

Also Called (List Synonyms):

Brn 1742652
Alfol 14
C14 Alcohol
Dytol R-52
Ec 204-000-3
Fatty Alcohol(C14)
Lanette K
Lanette Wax Ks
Loxanol V
Myristic Alcohol
Myristyl Alcohol
Tetradecanol
N-Tetradecanol
N-Tetradecanol-1
Tetradecyl Alcohol
N-Tetradecyl Alcohol
1-Hydroxytetradecane

Chemical Structure:



Suitable analogs or moieties of chemicals used in this assessment (CASRN(s)):
Linear long-chain (C6-C22) alcohols are frequently discussed herein as analog compounds for 1-tetradecanol. These alcohols have the same structural features and moieties, similar metabolic pathways, a common mode of ecotoxicological action and common levels and mode of human health related effects. Toxicological endpoints for linear long-chain alcohols have been observed to be qualitatively and quantitatively similar (OECD SIDS, 2006).

Chemical Structure(s) of suitable analog(s) and/or moieties:

Long Chain Alcohols (C6-22 primary aliphatic alcohols)

$CH_3(CH_2)_nCH_2OH$ Linear (n=4 to 20)

For Inorganic Chemicals and relevant particulate organics (*if not relevant, list NA*)

Define Properties:

1. Particle size (e.g., silica of respirable size) NA
2. Structure (e.g., amorphous vs. crystalline) NA
3. Mobility (e.g., water solubility, volatility) See Persistence section
4. Bioavailability
   - Data are available from a well conducted *in vitro* study using human skin in which myristyl alcohol (C14-alcohol, tetradecan-1-ol) gave a percutaneous absorption rate of 1.2% at 6 hours and 6.3% at 24 hours. Short-chain aliphatic alcohols are known to be rapidly and extensively absorbed from the gastrointestinal tract. The higher carbon number alcohols, from C9 upwards, are of low water solubility and have a partition coefficient which is greater than 4, so little systemic exposure would be expected following inhalation exposure (ECHA 2019a).

Identify potential applications/functional uses of the chemical:

- 1-Tetradecanol is a white solid or crystal used in organic synthesis, plasticizers, antifoaming agent, intermediate, perfume fixative for soaps and cosmetics, wetting agents and detergents, ointments and suppositories, shampoos, toothpaste, cold creams, and specialty cleaning preparations. 1-tetradecanol and 1-dodecanol are also used in combination with the (E, E) -8, 10-dodecadiene-1-ol, (Z)-11-tetradecene-1-yl acetate, and (Z)-9-tetradecene-1-yl acetate as a pheromone confusion mixture for controlling pests on plants, e.g., codling moths and leaf wrappers. In Denmark, the product is used for insect control in apples and pears. It is registered for pesticide use in the U.S. but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses. 1-Tetradecanol has been tested as experimental medication in controlling the progression of chronic periodontal disease (HSDB 2015).

Table 2. Environmental Transformation Products Summary

Life Cycle Stage	Transformation Pathway	Environmental Transformation Product	CAS #	Feasible (Yes or No)	Relevant (Yes or No)	GreenScreen List Translator Score or GreenScreen Benchmark Score
End of Life	Ultimate biodegradation	CO_2	124-38-9	Y	N	LT-UNK
		H_2O	7732-18-5	Y	N	BM4

Report rationale for each determination as to whether an identified environmental transformation product is feasible and relevant:

Bacteria will reduce aliphatic alcohols via b-oxidation to CO2 and H20 (Mudge 2005). These two ultimate biodegradation products are not considered relevant based on GreenScreen guidance (Section 14.3.2 Step 2; GreenScreen Method 2015).

HAZARD CLASSIFICATION SUMMARY

GROUP I HUMAN HEALTH EFFECTS (GROUP I HUMAN)

Carcinogenicity (C): *L*

Tetradecanol was assigned a hazard classification level of Low with low confidence for carcinogenicity based on negative findings for the chemical group long chain aliphatic alcohols (LCAAs). Specifically this group of chemicals are non-genotoxic and lack structural elements of concern for interaction with DNA. Together with the lack of response upon repeated application the skin painting studies LCAAs are regarded to be of little concern regarding carcinogenicity. The large set of various types of repeated dose studies across the category which do not offer any evidence of treatment-related induction of hyperplasia/pre-neoplastic lesions for any of the structurally related alcohols (though reporting is limited in many cases), and the lack of genotoxic effects demonstrated across the category, suggest that none of the category members are likely to be carcinogenic. The low hazard conclusion is based on weight of evidence which includes non-traditional carcinogenicity studies and conclusions made based on the LCAA chemical class and therefore is reported with low confidence.

Data

- Lists
  - *Authoritative:* not included on any authoritative lists
  - *Screening:* not included on any screening lists

- Measured Data

  ECHA 2019a
  - Several members of the category of the LCAAs have been tested as control substances in skin painting studies. Even taking into account the limitations of these experiments, the data show that none of aliphatic alcohols tested have a potential to induce local skin tumours upon repeated dermal application at or above the maximum tolerated (irritant) dose. Most of the study protocols considered here have almost certainly induced considerable local effects, however details of the irritation responses are limited and were reported only in a few cases. Irrespective of the causative agent, irritation at the site of application is a significant confounder in skin painting studies and its role in the tumour development of non-genotoxic chemicals has been well established.
  - LCAAs are non-genotoxic and lack structural elements of concern for interaction with DNA. Together with the lack of response upon repeated application the skin painting studies LCAAs are regarded to be of little concern regarding carcinogenicity. The large set of various types of repeated dose studies across the category which do not offer any evidence of treatment-related induction of hyperplasia/pre-neoplastic lesions for any of the structurally related alcohols (though reporting is limited in many cases), and the lack of genotoxic effects demonstrated across the category, suggest that none of the category members are likely to be carcinogenic.

ECHA 2019b

- Hexan-1-ol, octan-1-ol, decan-1-ol, dodecan-1-ol, tetradecan-1-ol, hexadecan-1-ol and octadecan-1-ol were tested in one or more mouse skin painting studies using applications two to three times weekly for periods up to sixty to seventy weeks. Development of local skin tumors was not reported in any of these assays. All of these experiments were conducted as part of investigative studies into co-carcinogenicity or tumor promotion properties of LCAAs (Sicé, 1966; Bingham, 1969; Van Duuren, 1976).
- Several members of the category of the LCAAs have been tested as control substances in skin painting studies. Even taking into account the limitations of these experiments, the data show that none of aliphatic alcohols tested have a potential to induce local skin tumors upon repeated dermal application at or above the maximum tolerated (irritant) dose. However, these data are unsuitable to assess properties such as co-carcinogenicity or tumor promotion for this category. Most of the study protocols considered here have almost certainly induced considerable local effects, however details of the irritation responses are limited and were reported only in a few cases. Irrespective of the causative agent, irritation at the site of application is a significant confounder in skin painting studies and its role in the tumor development of non-genotoxic chemicals has been well established (for examples see Nessel et al., 1998, 1999; Argyris, 1985). LCAAs are non-genotoxic and lack structural elements of concern for interaction with DNA (Ashby and Tenant, 1991). Together with the lack of response upon repeated application the skin painting studies LCAAs are regarded to be of little concern regarding carcinogenicity. The large set of various types of repeated dose studies across the category which do not offer any evidence of treatment-related induction of hyperplasia/pre-neoplastic lesions for any of the structurally related alcohols (though reporting is limited in many cases), and the lack of genotoxic effects demonstrated across the category, suggest that none of the category members are likely to be carcinogenic.

MAK Value Documentation, 2006

- 1-Dodecanol is a co-carcinogen for benzo[a]pyrene in the mouse. The tumor-promoting effects on the mouse skin are, despite the irritation, negligible.
- In a carcinogenicity screening test for lung adenomas according to Shimkin, groups of 15 A/He mice per sex and dose were given intraperitoneal injections of 1-dodecanol of 100 or 500 mg/kg body weight in tricaprylin 3 times a week for 8 weeks. No increase in lung tumors was observed at the end of the study 24 weeks after the first injection (Stoner et al. 1973). This method is, however, not a usual test, as it is substance class specific and not a validated carcinogenicity bioassay.

OECD SIDS 2006a

- 50 mice aged 6-8 weeks treated 3 times weekly by skin application with 10 mg Dodecanol in acetone, 0.1 ml for 440 days. Another group of 50 animals received the same dose of dodecanol but were also exposed to B[a]P, 5 ug/0.1 ml in acetone 3 times weekly. During the experimental period animals bearing tumors appearing grossly to be carcinomas were killed 2 months after the tumor was classified as malignant, or when animals were moribund. All animals were autopsied. *No tumors were observed in the 50 mice receiving dodecanol.* Of the animals receiving dodecanol and B[a]P, 27 papillomas occurred in a total of 21 animals, 13 mice with

squamous cell carcinoma. In a control group also consisting of 50 mice and being treated with B[a]P (5 ug) alone, 26 papillomas were observed in 16 animals, 12 of these tumors being squamous cell carcinoma. The authors conclude that these results suggest a weak to moderate cocarcinogenic effect.
    - Groups of 20 animals each were exposed by skin application to 50 mg of a solution of 0.05%, or 0.2% Benzo[a]pyrene in decalin twice weekly, which had been adulterated with 0, 10, 20, 30, 40, 50, 75 or 100% dodecanol. Test results: Malignant tumors occurred in 65-100% of all 16 groups. In the animals exposed to 0.05% B[a]P, the tumor latency period decreased steadily from 63 weeks for mice receiving no dodecanol, to 26 weeks for mice exposed to the solution containing 100% dodecanol. In the groups exposed to 0.2% B[a]P, average latency decreased from 42 weeks in the group receiving no dodecanol, to 22 weeks in the 100% dodecanol group. There were no skin tumors seen in 50 control animals receiving 50% dodecanol in decalin alone.

- Estimated Data – None

Mutagenicity/Genotoxicity (M): L

Tetradecanol was assigned a hazard classification level of Low for Mutagenicity/Genotoxicity based on negative findings in both *in vitro* and *in vivo* studies. In addition, as a chemical group long chain aliphatic alcohols (LCAAs) are non-genotoxic and lack structural elements of concern for interaction with DNA. The lack of genotoxic effects demonstrated across the category, suggest that none of the category members are likely to be Mutagenicity/Genotoxicity. The low hazard conclusion is based on study data specific to the chemical and therefore is reported with high confidence.

Data
- Lists
    - *Authoritative:* not included on any authoritative lists
    - *Screening:* not included on any screening lists

- Measured Data
  ECHA 2019a
    - In a reliable study, conducted in accordance with OECD guideline 471 and under GLP, the C14 alcohol Kalcol 4098 did not increase the reverse mutation rate in histidine dependent bacterial strains of Salmonella typhimurium in the presence or absence of metabolic activation at concentrations up to 5000 µg/plate. The top concentration was not cytotoxic. It is concluded that the test substance is not mutagenic to bacteria under the conditions of the test.
    - Fatty alcohol blend has been tested according to OECD 474 and under GLP. Male and female mice were dosed with 500, 1000 and 2000 mg/kg bw. No increase in the number of micronucleated PCE was observed (1000 PCE scored per animal). It is concluded that the test substance is negative for the induction of micronuclei under the conditions of the test. No toxicity to bone marrow or general toxicity was observed.
    - In a reliable study, conducted according to OECD guideline 474, no genotoxicity was seen in mice after a single oral dose of 5000 mg/kg bw. The study was performed in

compliance with GLP.

- An *in vitro* cytogenicity study was conducted on C12-C13 linear chain alcohols with CHO cells. The test substance was evaluated at concentrations up to cytotoxic levels with and without S9 activation. No significant increase in chromosome aberrations, polyploids or endoreduplicates was observed at any dose level with and without S9 activation. A repeat experiment confirmed these results and C12-C13 linear chain alcohols tested negative for genotoxicity.
- An *in vitro* gene mutation study (reliability 2) was conducted on 1-tetradecanol. Concentrations of 50, 150, 500, 1500, and 5000 µg/plate were evaluated with and without metabolic activation for an exposure duration of 48 hours. These same conditions were applied to two strains of bacteria. No significant increase in mutation rate was detected and 1-tetradecanol was determined not to be mutagenic at any of the concentrations tested.
- A C6-C24 fatty alcohol blend was tested according to protocol similar to OECD 476 and under GLP. Bacterial assays were exposed to test substance concentrations of 0.4, 4.3, 43.2, 432, and 4320 µg/ml and 9.4, 18.8, 37.5, 75, 150, 300 µg/ml. No increase in mutant frequency resulted with or without metabolic activation throughout original and repeat experiments. The test substance was concluded to be negative for mutagenicity under the conditions of the test.

HSDB

- In the only GLP test for in vivo genetic toxicity (OECD 474) no statistically significant effects were noted in mice which had received oral doses of 5000 mg/kg. This study is assumed to be the most reliable and is taken as evidence that 1-Dodecanol is not mutagenic in vivo.

MAK Value Documentation, 2006

In vitro

- 1-Dodecanol was not found to be mutagenic in the Salmonella mutagenicity test with strains TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of a metabolic activation system (S9 fraction from the livers of rats treated with Aroclor 1254) in concentrations of 4, 20, 100, 500 or 2500 µg/plate as a suspension in water using Tween 80. After doses of 100 µg/plate or more, 1-dodecanol had toxic effects (Henkel 1982). 90 % 1-dodecanol was not found to be mutagenic in the Salmonella mutagenicity test with strains TA98, TA100, TA1535, TA1537 and TA1538, and Escherichia coli (WP2uvrA) in the presence and absence of a metabolic activation system (S9 fraction from the livers of rats treated with polychlorinated biphenyls (KC 500)) in concentrations of 0.01, 0.05, 0.1, 0.5 1, 5, 10 or 50 µg/plate in DMSO. With strain TA1535 growth inhibition was observed after concentrations of 10 µg/plate or more, with the other strains after 50 µg/plate or more (Shimizu et al. 1985)

In vivo

- In a micronucleus test according to OECD test guideline 474, no significant increase in the incidence of micronuclei was observed after mice were given gavage doses of 1-dodecanol of 5000 mg/kg body weight in arachis oil. The batch investigated was 100 % pure. Neither an increase in mortality nor a decrease in the ratio of polychromatic to normochromatic erythrocytes was observed (Henkel 1992).

OECD SIDS 2006a

- In the Russian literature, Lauryl alcohol was reported to diminish cell mitotic activity and cause structural changes to chromosomes and the mitotic apparatus in Vicia faba after 14 hours exposure. It was not possible to further evaluate the significance of this finding
- Another Russian article reports chromosomal aberrations in 3.6% of 500 cells examined in rats exposed orally to 1/5 of the LD50 dose of n-Dodecanol (versus None in 600 cells from non-exposed animals). It was not possible to further evaluate the significance of this experiment.
- Various *in vivo* tests on long chain alcohols in the range C6-C22, including 1-tetradecanol, were negative for genetic toxicity. The details of these studies are not included in the publication
- Two *in vitro* genetic toxicity studies were performed on 1-tetradecanol over concentration ranges of 15-5000 µg/plate and 50-5000 µg/plate with and without activation. Under all conditions tested, no increase in reverse mutation rate was observed and 1-tetradecanol was determined not to by cytotoxic.

OECD SIDS 2006b

- Long chain aliphatic alcohols do not contain structural elements of concern for potential interaction with DNA and have been shown to be without mutagenic activity, primarily on the basis of Ames assays and mouse micronucleus assays.

- Estimated Data - None

Reproductive Toxicity (R): L

Tetradecanol was assigned a hazard classification level of Low with high confidence for reproductive toxicity. The hazard score is based on negative findings for a high-quality analog in OECD reproductive/developmental toxicity screening study and repeat dose studies in multiple species that reported no effects to reproductive organs. While study data specific to tetradecanol was not available, the negative conclusions are reported for high quality chemical analogs. Specifically, as a chemical group long chain aliphatic alcohols (LCAAs) as a category are considered without a potential for adverse effects on fertility and reproductive toxicity. The low hazard conclusion is based on study data specific to the chemical and therefore is reported with high confidence.

Data

- Lists
  - *Authoritative:* not included on any authoritative lists
  - *Screening:* not included on any screening lists

- Measured Data

ECHA 2019a

- The NOAEL for effects on the reproductive organs of dogs is >1054 mg/kg/day (3% in the diet). There were no treatment related effects on reproductive organ weights and no histopathological changes in the gonads of top dose animals. This is also the NOAEL for systemic toxicity.

ECHA 2019b

- Dodecan-1-ol has been tested for potential reproductive toxicity in a combined

repeat dose reproductive/developmental toxicity screening study in rats conducted according to the draft OECD guideline 422 and in compliance with GLP. The materials were administered to male and female rats via the diet at concentrations up to 30,000 ppm (2000 mg/kg bw/day) during pre-mating, mating and gestation. Pregnancy rates, uterine parameters, time to pregnancy and gestation length indicated that fertility was not affected by exposure to octadecan-1-ol. There were no microscopic changes observed in the reproductive organs. *It should be noted that it is unclear in ECHA entry exactly what long chain aliphatic alcohol is being reported in this study. However, both Dodecan-1-ol and octadecan-1-ol have been studied for repro/dev toxicity by Hansen in 1992.*

- Following repeated oral administration of equimolar dose levels of various alkanols to male rats for a period of 14 days there were no statistically significant differences in body weight gain, or relative liver or testes weights.
- In a reliable screening study, performed using a protocol similar to OECD guideline 407, the 28-day oral NOAEL for effects on reproductive organs in rats was determined to be 1000 mg/kg bw/day.
- A read across feeding studies reported a lack of effects on the reproductive organs of rats receiving hexan-1-ol (NOAEL 1127 mg/kg). No adverse effects were noted at any of the dose levels administered during the study. No effects in reproductive organs have been observed in repeated dose studies with any category member.

OECD SIDS 2006b

- In a 13-week rat study C14-16 alcohol (mainly C14and C15 alcohols; linearity 70%) was administered via the diet at concentrations of 0, 0.2, 1 and 5%. The top and intermediate dose level (5 and 1%, respectively) had limited palatability and induced a considerable reduction in growth (> 30% and ca. 15% reduction in body weight in high and mid dose males, respectively). No treatment-related microscopic changes were observed, including both the testis and ovaries at this same dose level.
- Tridecanol [CAS 112-70-9] 1-tridecanol was shown to be without a potential for peroxisomal proliferation or hypolididaemia. No histological or weight changes were observed in the liver and testes after oral administration of 184 mg/kg/day for 2 weeks (Rhodes et al., 1984).
- Not expected to impair fertility
- On the basis of the lack of adverse findings in the reproductive organs in repeated dose toxicity studies and in screening studies for reproductive effects this category (long chain aliphatic alchohols) is considered without a potential for adverse effects on fertility and reproductive toxicity.

- Estimated Data

Developmental Toxicity incl. Developmental Neurotoxicity (D): L

Tetradecanol was assigned a hazard classification level of Low with high confidence for developmental toxicity incl. developmental neurotoxicity. The hazard score is based on negative findings using high quality analogs in OECD reproductive/developmental toxicity screening studies. While study data specific to tetradecanol was not available, the negative conclusions are reported for high quality chemical analogs. Specifically, toxicity studies in substances belonging to the long chain alcohol category have confirmed the lack of potential adverse effects on the developing fetus. The low hazard

conclusion is based on study data specific to the chemical and therefore is reported with high confidence.

Data

- Lists
  - *Authoritative:* not included on any authoritative lists
  - *Screening:* not included on any screening lists

- Measured Data

  ECHA 2019a
  - Read across data from a combined repeat dose and reproductive/developmental toxicity screening study reported a lack of effects on the reproductive organs of male and female rats receiving dodecan-1-ol (NOAEL > 2000 mg/kg/bw). This study also reported a NOAEL for developmental effects to be 2000 mg/kg/bw.

  ECHA 2019b
  - In a reliable study, conducted according to a protocol similar to OECD guideline 414, the NOAEL for maternal toxicity, teratogenicity and fetotoxicity in rabbits, was 2000 mg/kg/day (highest dose tested). The study was performed in compliance with GLP.
  - In a reliable study conducted to the draft OECD guideline 422, the rat NOAEL for maternal and developmental toxicity was 2000 mg/kg bw/day, the highest dose tested. The study was performed in compliance with GLP. There was no reported statistically significant abnormalities in pups
  - In a reliable study, performed to OECD guideline 414, an NOAEL of 130 mg/kg bw/day (the lowest dose tested) was determined for maternal toxicity and an NOAEL of 1300 mg/kg bw/day for teratogenicity and fetotoxicity (the highest dose tested). The study was performed in compliance with GLP. Administration of octan-1-ol to rats at daily gavage doses of 0, 130, 650, 975 or 1300 mg/kg resulted in significant, dose-related maternal toxicity, including clinical signs (depression, nasal discharge and pneumonia), and slight decreases in body weight gain and food consumption at 650, 975 or 1300 mg/kg/day. No adverse effects were recorded on foetal and developmental parameters.
  - In a reliable study, development was assessed as part of a combined repeat dose and reproductive/developmental toxicity study, conducted according to draft OECD guideline 422. The NOAEL for maternal and foetotoxicity in rats was 2000 mg/kg bw/day (highest dose level). There was no evidence of teratogenicity from the limited examination of the pups that was carried out. The result is read across from octadecan-1-ol (CAS 112-92-5). *It should be noted that it is unclear in ECHA entry exactly what long chain aliphatic alcohol is being reported in this study. However, both Dodecan-1-ol and octadecan-1-ol have been studied for repro/dev toxicity by Hansen in 1992.*

  OECD SIDS 2006b
  - Not expected to be a developmental toxicant in the absence of maternal toxicity
  - Developmental toxicity studies in substances belonging to the long chain alcohol category and aliphatic alcohols supporting this category studies have confirmed the lack of potential adverse effects on the developing foetus.

- Estimated Data - None

Endocrine Activity (E): DG

Tetradecanol was assigned a DATA GAP for Endocrine Activity based on lack of adequate studies. Endocrine activity data was reviewed for other long chain aliphatic alcohols; however, no data was located for any of these compounds.

Data

- Lists
  - *Authoritative:* not included on any screening lists
  - *Screening:* not included on any screening lists

- Measured Data
  MAK Value Documentation, 2006
  - An intraperitoneal dose of 500 mg/kg body weight was found to be the maximum tolerated dose in a dose-finding study for a short-term carcinogenicity test (Section 6.7), in which 15 A/He mice per dose group and sex were injected with a solution of 1-dodecanol in redistilled tricaprylin 3 times a week over a period of 8 weeks. The organs included in the microscopic and gross pathological examinations were the lungs, liver, kidneys, spleen, thymus, intestine, and salivary and endocrine glands (no other details; Stoner et al. 1973).

- Estimated Data - None

GROUP II AND II* HUMAN HEALTH EFFECTS (GROUP II AND II* HUMAN)

Note: Group II and Group II endpoints are distinguished in the v1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen Guidance v1.4, Annex 2 for more details.*

Acute Mammalian Toxicity (AT): L

Tetradecanol was assigned a hazard classification level of Low with high confidence for acute mammalian toxicity based on oral and dermal LD50 values > 2,000 mg/kg /L. In addition, acute mammalian toxicity studies in high quality analogs (substances belonging to the long chain alcohol category) have confirmed the low acute toxicity. The low hazard conclusion is based on study data specific to the chemical and therefore is reported with high confidence.

Data

- Lists
  - *Authoritative:* not included on any authoritative lists
  - *Screening:* not included on any screening lists

- Measured Data

  ECHA 2019a
  - In the acute oral toxicity study, 2000 mg/kg bw of test material in arachis oil was administered orally to 5 male and 5 female rats. During the 14 -day study period, the animals were weighed on days 0, 7 and 14 and any clinical and behavioral signs were noted regularly. Necropsy was performed at the end of the study period. There were no deaths during the 14 -day study period. An LD50 value of > 2000 was reported. The study was conducted according to an appropriate OECD test guideline and in compliance with GLP.
  - The rat 1-hour inhalational LC50 for tetradecan-1-ol is >1.5 mg/l.
  - The rabbit dermal LD50 (24 hour occluded) for Alfol 14 was approx. 8000 mg/kg. All survivors showed skin irritation at the application site throughout the observation period. Signs of intoxication included weakness, emaciation and pallor. The result is read across from tetradecan-1-ol (CAS 112-72-1).

  ECHA 2019b .
  - The rat oral LD50 for Lorol 8 was >5g/kg when applied as an aqueous suspension.
  - The rat oral LD50 for Safol(TM) 23 Alcohol C10-16 alcohols Type B (also known as Compound 33A) is >2000 mg/kg.
  - The rat oral of 3.21 g/kg was determined in a reliable study conducted according to an appropriate test protocol. Not conducted according to GLP.
  - The result was read across from 1-decanol. The rat 1-hour LC50 for Alfol 10 (mist) was >71 mg/l.
  - Rat 6-hour LC50 was reported to be >700mg/m3 air. The study was equivalent to guideline. The result was read across from undecan-1-ol (CAS 112-42-5)
  - The rat 1-hour inhalational LC50 for tetradecan-1-ol is >1.5 mg/l.
  - The rabbit dermal LD50 (24 hour occluded) for Alfol 14 was approx. 8000 mg/kg.

The result is read across from tetradecan-1-ol (CAS 112-72-1).
- The rat dermal LD50 value of >5000 mg/kg is reported in a reliable study conducted according to an appropriate guideline. The study was compliant with GLP.
- In an acute dermal toxicity study, the test material (icosan-1 -ol) was applied onto rabbit skin and kept in contact to the skin for 4 hours under occlusive dressing. There is lack of detail on the materials and methods used, as well as results, however the study reports an LD50 value of > 20 ml/kg (>16,800 mg/kg using the density of 0.84 g/cm3).

HSDB
- LD50 Rat oral 5 g/kg
- LD50 Rabbit dermal >5 g/kg

Pubchem 2019
- LD50 Rat oral 12,800 mg/kg
- LC50 Rat inhalation >1050 mg/cu m (138 ppm)
- LD50 Guinea pig dermal >8310 mg/kg

- Estimated Data

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-single) L

Tetradecanol was assigned a low with high confidence for single dose systemic toxicity/organ effects. The hazard score is based on no indication of specific target organ toxicity reported following oral, inhalation or dermal oral exposures. In addition, acute studies in high quality analogs (substances belonging to the long chain alcohol category) have confirmed the low single dose systemic toxicity/organ effects. While some minor lung congestion was noted in rats exposed to very high inhalation concentrations this effect is determined to be not of toxicological significance and was only observed to occur at very high concentrations. The low hazard conclusion is based on study data specific to the chemical and therefore is reported with high confidence.

Data
- Lists
  - *Authoritative:* not included on any authoritative lists
  - *Screening:* not included on any screening lists

- Measured Data

  ECHA 2019a
  - In the acute oral toxicity study, 2000 mg/kg bw of test material in arachis oil was administered orally to 5 male and 5 female rats. During the 14 -day study period, the animals were weighed on days 0, 7 and 14 and any clinical and behavioral signs were noted regularly. Necropsy was performed at the end of the study period. There were no deaths during the 14 -day study period. No signs of systemic toxicity were noted and all animals showed the expected body weight gain during the study period. No abnormalities were noted at necropsy. The study was conducted according to an appropriate OECD test guideline and in compliance with GLP.
  - Following rat 1-hour inhalational pf tetradecan-1-ol is at 1.5 mg/l there were no signs of toxicity and findings at gross necropsy were unremarkable.
  - In the acute dermal toxicity study, 2, 4 and 8 g/kg of test material was applied to the

flanks of 2 male and 2 female rabbits per dose, kept in contact to the skin under occlusive dressing for 24 hours. The experiment was performed on intact and abraded skin. Body weight changes and clinical signs of toxicity were noted regularly. Necropsy was performed at the end of the 14 -day study period. 100% of the animals with abraded skin died between 8 and 10 days of the exposure period. The animals with intact skin survived. At twenty-four hours following test application, all animals showed slight to moderate erythema, desquamation, wrinkling and dryness of the skin at the treatment site. In all surviving animals, desquamation and wrinkling of the skin occurred and persisted in varying degrees throughout the 14 -day study period. At the highest dosage level (8 g/kg body weight, two of the surviving animals showed signs of weakness, emaciation and pallor; however, all appeared systematically normal within 96 hours following exposure. Final body weight records of the surviving animals at termination, showed a slight loss in one animal, a constant weight in one animal and gains within expected limits in the eight remaining animals. At necropsy, there was one animal with slight accumulation of clear viscous fluid within the peritoneal cavity and crazing over cortex of both kidneys. Eight animals showed no signs of gross systemic abnormalities.

ECHA 2019b

- OECD Guideline 401 (Acute Oral Toxicity) in rats, there were no deaths or clinical signs of toxicity at a dose level of 2000 mg/kg bw.
- When applied as an aqueous suspension Lorol 8 at 5g/kg produced no remarkable gross pathology at necropsy in rats and no indication of specific target organ toxicity
- In an acute oral toxicity study, 2000 mg/kg of test material dissolved in arachis oil was administered to 5 male and 5 female rats. Body weight changes and clinical signs of toxicity were noted regularly during the 14 -day study period. Necropsy was performed at the end of the study. There were no deaths during the 14 -day study period. No signs of systemic toxicity were observed. The expected gain in body weight was observed in all animals. No macroscopic abnormalities were observed at necropsy.
- The rat oral LD50 for Safol(TM) 23 Alcohol C10-16 alcohols Type B (also known as Compound 33A) is >2000 mg/kg. There was no target organ toxicity. Findings at gross necropsy were unremarkable.
- The result was read across from 1-decanol. The rat 1-hour LC50 for Alfol 10 (mist) was >71 mg/l. Gross necropsy revealed congestion of the lungs in all animals.
- Rats exposed to 700mg/m3 air undecan-1-ol (CAS 112-42-5). Upon removal from the chamber the fur was roughened; respiration was normal, and no other signs of toxic distress were noted. The ten-day observation period was uneventful.
- Rats exposed for 1-hour inhalational to tetradecan-1-ol at 1.5 mg/l. There were no signs of toxicity and findings at gross necropsy were unremarkable.
- 4-hour rat exposure to >0.237 mg/l Dobanol 91 (near saturated vapor concentration) produced no signs of toxicity at this exposure level.
- No gross abnormalities were noted for any rats when necropsied at the conclusion of the 14-day observation period following dermal exposures to the substance at 5000 mg/kg observation period.
- No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

MAK Value Documentation, 2006

- 63 Sprague-Dawley rats were exposed to an aerosol of 1-dodecanol in a concentration of 1050 mg/m^3 for 6 hours. All animals survived the treatment. Only in

a few animals were slight, unconnected areas of lung hemorrhage seen at autopsy (only lungs and trachea).
- In an acute oral study with 7 rabbits and 7 rats which survived oral administration of technical grade 1-dodecanol in doses of up to 36 ml/kg body weight (29900 mg/kg body weight), gross pathological and microscopic examination of the organs did not yield unusual findings (no other details). In one rat, which died 6 days after oral administration of 36 ml/kg body weight, fatty degeneration of the liver and confluent bronchopneumonia were found (Rowe and McCollister 1982).
- In another study according to OECD test guideline 401, marked piloerection and slight sedation were observed about 20 minutes after gavage administration of 5000 mg/kg body weight in the form of an aqueous suspension. The symptoms had regressed completely 24 hours after administration of the substance. Other symptoms were not detected in either the first 24 hours, or 7 and 14 days after administration. All animals survived the treatment. Autopsy did not yield conspicuous findings in the inner organs and body cavities (Henkel 1981a).

- Estimated Data - None

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-repeat) (Group II*) L

Tetradecanol was assigned a low with high confidence for Repeat Dose Systemic Toxicity/Organ Effects incl. Immunotoxicity. The hazard score is based on limited effects reported using high quality analogs following oral and dermal exposures. Specifically, no significant toxicity was observed following rat oral exposures at concentrations >100 mg/kg and dermal doses of > 200 mg/kg/bw. While study data specific to tetradecanol was not available, the no significant toxicity conclusions are reported for high quality chemical analogs. While oral and dermal exposures to other long chain aliphatic alcohols were noted to have some effect on body weights, liver enzymes or total white blood cell counts, these effects were considered not adverse as there was no associated pathology. Specifically, these effects are reported to have occurred in the absence of histopathological alterations and therefore assumed to be of limited toxicological significance. The hazard score is based on study data in high quality analogs and therefore is reported as high confidence

Data
- Lists
  - *Authoritative:* not included on any screening lists
  - *Screening:* not included on any screening lists

- Measured Data
  ECHA 2019a
  - The key study was performed using a protocol similar to OECD guideline 408 but prior to the introduction of GLP. The test material Alcohols, C14-15 branched and linear was administered to rats via the diet for 90 days at concentrations of 0, 0.2, 1 and 5% (providing average intakes of 169, 747 or 3548 mg/kg bw/day, respectively). The top and intermediate dose level (5 and 1%, respectively) had limited palatability and induced a considerable reduction in growth (>30% and approx. 15% reduction in

body weight in high and mid dose males, respectively). Biochemistry showed increased liver enzyme activity (alkaline phosphatase and alanine aminotransferase) at the 1 and/or 5% level. It is considered that the increases in hepatic enzymes are not adverse as there was no associated pathology. The increase in relative weights of a number of organs is attributable to the reduced body weight due to lower food consumption as a result of lack of palatability. No treatment-related microscopic changes were observed, including both the testis and ovaries at this same dose level. Based on the effect on body weight a NOAEL was established at the 5% dietary incorporation level (3548 mg/kg).

ECHA 2019b

- In a reliable study, in which rats were treated with Alfol 16 via the diet for 13 weeks, *an NOAEL of >4400 mg/kg bw/day* (highest dose tested) was determined. Reduced weight gain, food consumption and organ weight changes were deemed to be secondary to the high dose administered but not specific to the test substance.
- Rats exposed to hexan-1-ol via the diet for 13 weeks showed no signs of significant toxicity when administered at nominal concentrations up to 1% (with staged increases at concentrations up to 6% during the last phase of the exposure period). There were no microscopic alterations recorded in the animals receiving concentrations of 6% (*equivalent to 1127 mg/kg/day*).
- The No-Observed-Effect-Level (NOEL) following dermal administration of fatty alcohol blend for a minimum of 90 days was stated to be less than 100 mg/kg/day. The clinical signs reported in this study such as effects on body weight and food consumption are considered to be a consequence of the local irritant effect and the effects on white blood cell counts and albumin and globulin levels attributable to the acute dermal inflammatory response. The increased adrenal weights (with no associated pathological changes) were attributed to a stress response, also as a result of the dermal irritation. Therefore, these effects are secondary to the local irritant effect of fatty alcohol blend. There were also changes to some clinical chemistry parameters noted (decreased glucose and calcium, increased urea nitrogen, alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase). The magnitude of change was generally not marked and/or was without pathological correlate in all cases and so they were considered not be adverse. Therefore, as there were no systemic effects noted that could not be attributed to the local irritant response, or were considered to be adverse, the systemic No-Observed-Adverse-Effect-Level following dermal administration of fatty alcohol blend for a minimum of 90 days was considered to be *1000 mg/kg/day (the highest dose tested*).

OECD SIDS

- Tridecanol [CAS 112-70-9] 1-tridecanol was shown to be without a potential for peroxisomal proliferation or hypolididaemia. No histological or weight changes were observed in the liver after oral administration of 184 mg/kg/day for 2 weeks (Rhodes et al., 1984).
- Repeated dose toxicity: OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test. 24 rats (12 male and 12 female) were used in each dose group, which received 1-Dodecanol in the diet in concentrations of 0, 1500, 7500, and 30000 ppm (ca. 0, 100, 500 and 2000 mg/kg/bw/day) for a period of 37 days. 1-Dodecanol had no influence on body weight, weight gain, food consumption and food efficiency in either sex at the doses

employed. All pathological and histopathological findings were considered incidental, and not related to the dosing. Except for the small effect on white blood cells and biological parameters mentioned above, no toxic effects were observed. No gross pathological or histopathological effects at doses of 0, 100, 500 or 2000 mg/kg in the feed. The total number of white blood cells was slightly reduced, from 7.0 in controls, 5.9 at 100 mg/kg, 4.3 at 500 mg/kg (P<0.001) and 4.7 at 2000 mg/kg (P<0.01). No differences in the differential counts of WBC types was seen, and the toxicological significance of this finding is difficult to assess. In addition, plasma free cholesterol was reduced from a mean of 0.18 in controls to 0.11 in the 500 mg/kg group (P<0.05), and triglycerides were reduced from 0.58 in controls to 0.31 in the 2000 mg/kg group (P<0.01).

MAK Value Documentation, 2006

- One study, in which 10 % 1-dodecanol in the diet of male Wistar rats caused the death of all animals after 12 days while 5 % 1-dodecanol was tolerated well, is not included in the evaluation as the only parameters investigated were body weight gains and lethal toxicity, and there were not enough animals used (no other details; Yoshida et al. 1971).

- Estimated Data - None

Neurotoxicity (N-single) *M*

Tetradecanol was assigned a moderate with low confidence for single exposure neurotoxicity. The hazard score is based on reported transient narcotic effects such as hypoactivity and/or ataxia, lethargy and prostration following both inhalation and oral exposures to high quality analogs. These transient narcotic effects fulfill the criteria for GHS category 3 specific target organ toxicity following single exposure which is equivalent to a GreenScreen moderate hazard for this endpoint. While no data specific to tetradecanol was located the hazard score is based on study data for high quality analogs. The GHS Category 3, transient target organ effects for narcotic effects, classification is intended to be based primarily on human data and "Animal data may be included in the weight of evidence evaluation." The GHS Category 3 classification, which is based solely on animal studies, deviates from the GHS guidance due to lack of human data. Therefore the moderate classification is precautionary and is reported as low confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data

  ECHA 2019b
  - Rats orally exposed to Lorol 8 at 5g/kg in aqueous suspension showed clinical signs of intoxication such as slight sedation and piloerection during the first 24 hours following dosing.
  - Rats orally exposed to Safol(TM) 23 Alcohol C10-16 alcohols Type B (also known as Compound 33A) at 2000 mg/kg. showed transient signs of intoxication within a few

hours of dosing and included diarrhoea, piloerection and lethargy. Findings at gross necropsy were unremarkable.
- Rats orally dosed with 1.17, 1.65, 2.33, 3.28, 4.64 and 6.55 gm/kg 1-Dodecanol. Animals at all dose levels exhibited weakness and ataxia. They became comatose and breathing was labored while comatose. Animals which survived appeared normal within 24 hours other than top dose animals (6.55 g/kg) where the rats appeared unwell up to 48 hours after dosing.
- Inhalation exposure to >71 mg/l 1-decanol resulted in signs of intoxication during exposure including lethargy, and/or ataxia, salivation and gasping. Gross necropsy revealed congestion of the lungs in all animals.
- A 1-hour inhalation exposure to a mist of Alfol 6 of 21 mg/l. During exposure all animals showed hypoactivity and/or ataxia, lethargy and prostration. However, within 2 hours of removal from the exposure chamber the animals all appeared and continued to appear normal throughout the observation period
- 4h inhalation exposure in rats to 11.46 mg/L 1-Dodecanol. Following exposure all animals were hypoactive and exhibited abnormal respiration, hunched posture and/or nasal discharge. However, all animals recovered by day 7 and appeared active and healthy for the remainder of the 14-day observation period.

MAK Value Documentation, 2006
- In an acute oral rat study according to OECD test guideline 401, marked piloerection and slight sedation were observed about 20 minutes after gavage administration of 5000 mg/kg body weight in the form of an aqueous suspension. The symptoms had regressed completely 24 hours after administration of the substance. Other symptoms were not detected in either the first 24 hours, or 7 and 14 days after administration. All animals survived the treatment. Autopsy did not yield conspicuous findings in the inner organs and body cavities (Henkel 1981a).

- Estimated Data - None

Neurotoxicity (N-repeated) (Group II*) DG

Tetradecanol was assigned a DATA GAP for Neurotoxicity (N-repeated) based on lack of adequate studies. Neurotoxicity (N-repeated) data was reviewed for other long chain aliphatic alcohols, however, no data was located for any of these compounds.

Data
- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data

  OECD SIDS
  - Test substance: n-Lauryl alcohol, reagent grade. Test species/strain: Chicken, male white Leghorn. Test method: Groups of 15-16 1-day-old chicks fed 8-13% dodecanol in standard laboratory diet for three weeks. Test results: Mortality during the experimental period was about 20%. 23/94 chicks exhibited signs of encephalomalacia. Five of the animals showing symptoms were examined histopathologically, and in all cases necrotic lesions of the brain typical of nutritional

encephalomalacia were observed. Comments: The mean lethal dietary level of dodecanol for male Leghorn was determined as being 17.6% There were no deaths, and no cases of encephalomalacia in 15 chicks receiving 10% dodecanol in the diet, supplemented with 200 mg/kg feed of dl-a-tocopheryl acetate.

- Estimated Data - None

Skin Sensitization (SnS) (Group II*) L

Tetradecanol was assigned a low with high confidence for skin sensitization based on negative results reported in a single guideline studies for the compound and numerous studies for high quality analogs. Some positive reactions in high quality analogs have been noted but these are reported in studies that lack enough clinical detail or have are no data for the actual clinical relevance of the reactions found. In addition, positive reactions are primarily noted in patients were the skin barrier is impaired, as a result of their illness, and facilitates the penetration of potential allergens and thus sensitization. Therefore, the hazard score has been based on the results reported in the guideline studies reported in animals. The hazard score is based on a guideline study data and therefore is reported as high confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data

  ECHA 2019a
  - In a reliable study, conducted to OECD guideline 406, Kalcol 2098 was not a skin sensitizer in guinea pigs. The study was performed in compliance with GLP. The study is based on tetradecanol (CAS 112-72-1).
  - In a reliable study performed using a protocol similar to OECD guideline 406, Dobanol 25 was not sensitising to the skin of guinea pigs after a topical challenge with 2.5% when tested using the method of Magnusson and Kligman.
  - In a reliable study, conducted to a protocol similar to OECD guideline 406, Neodol 91 (1% in ethanol) was not sensitising to the skin of guinea pigs when tested using the Buehler non-adjuvant method. The study was performed in compliance with GLP.
  - In a reliable study, conducted to OECD guideline 406, Compound 33A (C10-16 alcohols Type B) was not a skin sensitizer when tested using a 100% challenge dose in a guinea pig maximization test. The study was performed to GLP.
  - A group of 20 test animals were treated with undiluted UDL-1635 for 6 hours once weekly for 3 weeks while a second group of 10 control animals were maintained without treatment until primary challenge application. Two weeks after the third induction exposure, both the test and control animals were challenged with 10% v/v solution of UDL-1635 in acetone. Only 1/20 animals in the test group showed a weak, non-persistent reaction suggestive of hypersensitivity during challenge at 24-hour reading. No positive responses were observed in the test animals at 48 hours

reading and in control animals. Therefore, it was concluded that UDL-1635 is not sensitizing according to EU criteria.

MAK Value Documentation, 2006

- The sensitization potential of a 1-dodecanol mixture before and after hydrogenation (see “Production”) was tested on guinea pigs previously sensitized with the raw material (no other details). The 1-dodecanol mixture before hydrogenation, in an aqueous vehicle, did not produce skin reactions in the patch test (concentration 0.33 %, 6 hours, read after 24 and 48 hours) in any of the 5 pre-sensitized animals. A solution of the 1-dodecanol mixture before hydrogenation, in 80 % aqueous ethanol vehicle, produced a reaction in 3 of 5 animals (concentration 0.33 %, 4 hours, read after 24 and 48 hours). Under these conditions, 1-dodecanol after hydrogenation also caused cross-reactions (Procter & Gamble 1999).
- Dodecanol is very probably an unimportant allergen. On the one hand, only relatively few cases have been observed despite the widespread use of the substance; on the other hand, studies are available from several independent centres, but mainly without clinically relevant data. In addition, the observed sensitization was mainly connected with previous illness, namely anamnestic or clinically manifest stasis eczema of the lower leg or venous ulcers.
- In persons with healthy skin, there was no evidence of allergenic effects either in a maximization test or a patch test with a sufficiently high concentration in a suitable vehicle (Kligman 1966, 1998, Komamura et al. 1997, Opdyke 1973a, 1973b). In collectives of patients the percentage of reactions in patch tests varies depending on the test concentration (e.g. very high test concentration in Auth et al. 1984), vehicle and selection of the patients. The collectives of patients were either patients with contact dermatitis or patients with anamnestic or clinically manifest venous ulcers or stasis eczema of the lower leg. With the consecutive testing of patients with existing contact dermatitis of different genesis (Hjorth and Trolle-Lassen 1963, Peter et al. 1969) on the one hand the numerous reactions may have been induced by a reduced irritation threshold, which led to false positive reactions which were in fact irritative (Kligman 1998). On the other hand, in these consecutive test studies there are no data for the actual clinical relevance of the reactions found. In addition, the skin barrier is impaired in these patients, as a result of their illness, and facilitates the penetration of potential allergens and thus sensitization. In patients with a history of ulcers, the occlusive treatment with local therapeutic agents can play a role as well. To what extent impurities are responsible for reactions to 1-dodecanol cannot be seen from the studies available, as there are no details on purity in most publications.

OECD SIDS 2006a

- A maximization test carried out on 25 human volunteers using 4% 1-dodecanol in petrolatum produced no cases of sensitization
- Occasional allergic reactions to 1-Dodecanol following skin contact have been reported but appear to be rare (of 1,664 eczema patients patch tested with 5% lauryl alcohol in Vaseline, 4 reacted; at 10% concentration 15 reactions are reported - it is difficult to rule out the possibility that some of these were, in fact, irritative responses).

OECD SIDS 2006b

- Aliphatic alcohols do not have a skin sensitization potential in animals. Based on human evidence, the allergenic potency of this category is very low

- Estimated Data - None

Respiratory Sensitization (SnR) (Group II*) DG

Tetradecanol was assigned a DATA GAP for respiratory sensitization based on lack of adequate studies. Respiratory sensitization data were reviewed for other long chain aliphatic alcohols; however, no data were located for any of these compounds.

Data
- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data
- Estimated Data

Skin Irritation/Corrosivity (IrS) H

Tetradecanol was assigned a high with high confidence for skin irritation/corrosivity based on a moderate irritation reported following single dermal application of Alfol 14. This is supported by the Japan GHS category 2 classification for the substance. The hazard score is based on results from a reliable study reported using tetradecanol and therefore is reported as high confidence.

Data
- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening:*
    - *Japan – GHS – Skin corrosion / irritation – Category 2*

- Measured Data

  ECHA 2019a
  - Based on the erythema and oedema scores reported Alfol 14 would be considered a skin irritant according to EU criteria and a class 2 irritant according to GHS criteria. Individual 24+48+72 hour erythema scores were >2.3 in 5/6 animals while the group mean 24+48+72 hour score was also in excess of 2.3 (2.46).
  - Undiluted Lorol C12-98 did not produce any skin irritation in human volunteers following a 4-hour semi-occlusive exposure in a test based on OECD 404.
  - The C8 alcohol Kalcohl 0898 is not a skin irritant according to either EU criteria following a 4-hour semi-occlusive exposure. Kalcohl 0898 can be considered as a mild irritant under GHS criteria.
  - In rabbits Alfol 10 is classified as moderately irritating (Category 3 based on GHS) to the skin. Specifically, for the first 24 hours after patch removal, all ttreated sites exhibited well-defined erythema and very slight edema. The overall incidence and severity of irritation decreased gradually with time. All animals were free of dermal irritation by day 10 (study termination). Under the conditions of this study.

- Following a 4-hour occluded exposure to rabbit skin, LIAL 111 (C11) was not a skin irritant according to EU criteria (group mean 24+48+48 hour scores <2). With erythema scores all >=1.5 LIAL 111 is classifiable as a mild (slight) skin irritant according to the GHS.
- Kalcol 220-80 is not a skin irritant when applied to rabbit skin undiluted in a 4-hour semi-occlusive exposure. Group mean 24+48+72 hours were 0. In the skin irritation study 0.5g of test material was moistened with 0.5ml distilled water and applied onto the skin of 3 female rabbits and kept under semi-occlusive dressing for 4 hours. The exposure area was shaved from hair prior to the treatment. After 4 -hour exposure any residual test material was removed by gentle swabbing with cotton wool soaked in distilled water. The skin reaction was evaluated at 1h, 24 h, 48 h, 72 h after patch removal according to Draize scoring system. The mean primary dermal irritation index was 0. The study was conducted according to an appropriate OECD test guideline, and in compliance with GLP.
- Following a 4-hour semi-occlusive exposure of Kalcol 6098 to rabbit skin there was no evidence of skin irritation between 24 and 72 hours after patch removal. Kalcol 6098 is not a skin irritant according to EU or GHs criteria.

HSDB

- Slight to moderate irritation was noted when 1-dodecanol was applied for 24 hr under occlusive conditions to the skin of rabbits and mice. No irritation was observed when 1-dodecanol was applied to the skin of guinea pigs.
- Contact for 48 hours with 4% 1-dodecanol in petrolatum was not irritating to 25 human volunteers but marked skin irritation was noted when 25% 1-dodecanol in mineral oil was given in open contact with scarified skin of 5 to 10 volunteers once a day for 3 days.

MAK Value Documentation, 2006

- The undiluted substance is barely irritative in man after single applications. In the guinea pig and the hairless mouse, the irritation after single applications of the substance is likewise slight, but in the rabbit, the most sensitive species, it is moderate. After repeated contact, somewhat stronger skin irritation can occur.
- Slight irritative potential was detected for 1-dodecanol only in one 24-hour patch test with Japanese persons (see Table 1; Sato et al. 1996). This could not be verified in other patch tests (Basketter 1997, Henkel 1996, Kästner 1977, Opdyke 1973b). Likewise, no irritative reactions could be detected using Burckhardt's method with repeated nonocclusive application. Only in the Duhring chamber scarification test according to Frosch and Kligman was the substance classified as clearly irritative. With this test method, which was developed for testing weak irritants, the skin is abrased before the occlusive Duhring chamber is applied (Frosch and Kligmann 1976, 1977). Another study with patch testing, in which there was no significant difference between the results of the positive controls (20 % sodium dodecylsulfate) and those of the test group, is not included in the evaluation as a result of this methodological shortcoming (Henkel 1996, 1999). Skin irritation is to be expected after repeated use (dehydration dermatosis).
- The irritative effects of 1-dodecanol after single applications of the substance to the skin are slight. The rabbit as the most sensitive species reacted to undiluted 1-dodecanol with slight to moderate skin irritation. While even 50 % 1-dodecanol in petrolatum was still moderately irritative in the rabbit, guinea pigs and the hairless

mouse produced only slight irritation in a few cases in the same investigation. This very different sensitivity between the various species may be explained by the different permeability of the skin (Bartek et al. 1972, Hopf 1971, Kästner 1977, Motoyoshi et al. 1979, Phillips et al. 1972). In the rat, also a sensitive species with much greater permeability of the skin than humans, marked damage to the skin was observed after repeated application of undiluted 1-dodecanol (Bartek et al. 1972, Rieger et al. 1964).

OECD SIDS 2006b

- For the aliphatic alcohols in the range C6 – C11 a potential for skin irritation exists, without concerns for tissue destruction or irreversible changes. Aliphatic alcohols in the range C12 – C16 have a low degree of skin irritation potential; alcohols with chain lengths of C18 and above are non-irritant to skin.

- Estimated Data - None

Eye Irritation/Corrosivity (IrE): M

Tetradecanol was assigned a moderate with high confidence for eye irritation/corrosivity based on weight of evidence of mild to moderate conjunctival irritation reported following applications of long chain aliphatic alcohols in numerous animal species. This effect is fully reversible most studies within a 7-day time period and fulfills the criteria of a GHS category 2B (mildly irritating) substance. The hazard score is based on results from guideline studies for high quality analogs and therefore is reported as high confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening:*
    - *Japan - GHS - Serious eye damage / eye irritation - Category 2B*

- Measured Data

ECHA 2019a

- In the eye irritation study, fine powder of test material was applied into the eyes of 3 rabbits. Assessment of ocular damage/irritation was made approximately 1 hour, 24, 48- and 72-hours following treatment. Total observation period was 14 days. Diffuse corneal opacity was noted in 2 treated eyes at the 24, 48, and 72-hour observations. Iridial inflammation was noted in 2 treated eyes at the 24-hour observation and persisted in 1 treated eye at the 48- and 72-hour observations. Moderate conjunctival irritation was noted in all treated eyes 1 hour after treatment and persisted in 2 treated eyes at the 24- and 48-hour observations. Minimal conjunctival irritation was noted in 1 treated eye at the 24- and 48-hour observations and in 2 treated eyes at the 72 hour and 7-day observation. Overall irritation score: Maximum group mean score 27.3 at 24 hours. All corneal and iridial scores and scores for conjunctival chemosis were normal by day 7. Conjunctival redness persisted in 2 rabbits through day 7 but scores were 0 by day 14. The effects were therefore fully reversible.

ECHA 2019b

- OECD Guideline 405 (Acute Eye Irritation / Corrosion). Rabbits experienced mild to moderate erythema of the palpebral and bulbar conjunctivae, mild to moderate chemosis, mild mucoid discharge and a mild to moderate corneal opacity involving one-fourth to three-fourths of the corneal surface. By 72 hours, all test eyes showed improvement in the parameters of irritation in all but one animal. That one animal became worse and even developed mild iritis.
- The eye irritation study was read-across from the structurally analogous substance C12-16. The study conducted according to OECD TG 405, 1987 and in compliance with GLP, reports the substance, Alcohols, C12-16, to be not irritating to the eye under the conditions of the study.
- Undecyl alcohol is described as slightly irritating to the eye in this test. AVERAGE SCORE (24+48+72 hour) 10.7/110 combined cornea, iris and conjunctivae. Under GHS criteria the results suggest classification as mild. Under EU criteria undecyl would not be considered irritant. After 24 hours there was a gradual improvement through to 120 hours when the iris and cornea appeared normal.
- Kalcol 6098 is not an eye irritant according to EU or GHS criteria. All eyes were normal at 48 and 72 hours post instillation. The result is a read across from hexadecanol (CAS 36653-82-4)
- Kalcol 0898 is an eye irritant according to EU criteria based on individual mean 24+48+72 hour scores for iritis of >= 1 in all test animals. Iritis, slight to moderate conjuncitivitis and areas of very slight/slight corneal opacity during the first 72 hours. Very slight conjunctivitis observed in all 3 animals at days 8 and 15. Very slight conjunctivitis persisted in 2 animals until termination on day 22. Iritis persisted in one of these rabbits until day 22. This material is considered an eye irritant under GHS and to cause a risk of serious damage to eyes (EU) based on persistence of iritis (1 rabbit) and conjunctivitis (2 rabbits) to 22 days
- Safol(TM) 23 Alcohol C10-16 alcohols Type B (also known as Compound 33A) is not an eye irritant according to EU or GHS criteria.
- In the eye irritation study, single instillation of 0.1 ml of solid test material was performed into one eye of 1 female and 3 male rabbits. No washing was performed after exposure. The untreated eye was used as negative control. The test area was examined at 1, 24, 48- and 72-hours post-application. Draize scoring system was used to evaluate the eye irritation response. Moderate conjuctival irritation was observed in all animals 1-hour post-application. At 24 hours, mild to moderate conjuctival redness was observed and by 72 hours post-treatment the redness was not evident. The study reports the test material to be not irritating to eye. The study was conducted according to an appropriate OECd test guideline, and in compliance with GLP.

HSDB

- The substance /1-dodecanol/ induced only mild, reversable eye irritation in rabbits exposed to 0.1 mL of an alcohol mixture containing over 60% 1-dodecanol.

OECD SIDS 2006b

- The eye irritation potential for alcohols with a chain length of C12 and above has been shown to be minimal.
- Rabbit eye irritation scored according to Draize criteria. Test substance: A. Commercial Lauryl alcohol (natural source) containing C10 0.3%, C12 68.9%, C14 25.1%, C16 5.1%, C18 0.3% and 0.3% unidentified. B. Commercial Lauryl alcohol (synthetic source) containing C10 0.1%, C12 63.3%, C14 24.1%, C16 8.3%, C18

0.4% and 3.8% unidentified Product A, 3 animals dosed with 0.1 ml/unwashed and 3 animals with 0.1 ml/washed. Product B, 3 animals dosed with 0.1 ml/unwashed and 3 with 0.1 ml/washed. The undiluted test substance was introduced into the conjunctival sac of the right eye of each rabbit, after which the eyelids were held closed for approximately 1 second. Rabbits in the washed group received washout about 4 seconds following installation with 20 ml lukewarm tap water. The left eye served as a control for each rabbit. Maximum average irritation scores dor product A were 9.3 (unwashed) at 1 hour, and 8.7 (washed) at 1 hour. For product B maximum scores (unwashed) of 10, and 8.4 (washed) at 1 hour. Most scores returned to zero within 3-4 days, but in one animal 14 days were required. All animals appeared normal during the course of the study, except for one female in group A. (washed) which exhibited hair loss around the right eye on days 17 to 21, and one male in group B. (unwashed) which exhibited clear nasal discharge on days 3 to 9. Comments: The results indicate mild, mainly conjunctival irritation under the conditions of this study. An additional study of the same two product batches, using a low volume procedure (10 ul test substance per eye), gave Draize scores of zero for substance A., and 2.8 for substance B.

- Estimated Data - None

ECOTOXICITY (ECOTOX)

Acute Aquatic Toxicity (AA): *H*

Tetradecanol was assigned a high with low confidence for acute aquatic toxicity based on reported LC/EC50 values of 1<10 mg/L is studies using tetradecanol. It should be noted however that data for other long chain aliphatic alcohols (estimated, C12-14 alcohols) LC/EC50s of <1.0 mg/L. The hazard score is based on results from guideline studies. However due to the conflicting toxicity values for high quality analogs which correspond to a higher hazard rating the confidence level has been reported as low.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening:*
    - *DK-EPA - Danish Advisory List - Acute1 - Very toxic to aquatic life (modeled)*
    - *EC - CEPA DSL - Inherently Toxic in the Environment*

- Measured Data

  ECHA 2019a
  - A 96h LC50 of > 1.0 mg/L was determined for the effects of the test substance on the mortality of *O. mykiss*.
  - A reliable EC50 value of 3.2 mg/l has been determined for the effects of tetradecanol on the immobility of the freshwater invertebrate D. magna. The effects seen need to be treated with caution because the formation of droplets in most of the test concentrations. However, in the range of the limit of solubility (1.9 mg/l) only 10% mortalities were observed, therefore the EC50 is >Limit of Solubility.
  - A 72 h EL50 value of >10 mg/L has been determined for the effects of the filtered test substance on growth rate of the algae S. subspicatus. The value is much higher than the limit of solubility of the test substance (ca. 0.1-0.4 mg/L), therefore the test substance is not toxic at the LoS.

  ECHA 2019b
  - A reliable 96h LC50 of 1.01 mg/L has been determined for the effects of the test substance on mortality of the fish *Pimephales promelas*.
  - A 96-hour LC50 value of 5.7 mg/L was determined for the effect of the test substance on mortality of the fathead minnow *Pimephales promelas*
  - A 120-h LC50 of 3.4 mg/l based on mean measured concentrations has been determined for the effects of decanol on mortality of fathead minnow embryos.
  - A 48 h EC50 value equivalent to 0.765 mg/L has been determined for the effects of the test substance on immobilisation of *Daphnia magna*.
  - A 96h EC50 value of 20 mg/L has been determined for the effects of the test substance on immobility of the freshwater flea Daphnia magna.

  OECD SIDS 2006a
  - In Bluegill sunfish (*Lepomis macrochiris*) a 96-hour LC50 of 894 mg/l is reported (static) for an alcohol mixture containing 66% dodecanol.
  - Toxicity to Daphnids: DIN 38412 part 11 (approximates OECD 202, part 1) EC50 48 hour = 320 mg/l

- In a Harpticoid (*Nitrocra spinipes*) a 96-hour LC50's of 0.9mg/l and 1.0 mg/l were seen. In tadpoles (Rana pipiens, early pre-limb bud) loss of righting reflex was recorded at 0.88 mg/l and 1.0 mg/l in two experiments. 50% of Mosquito larva exposed to dodecanol floating on the water surface died at concentrations as low as 0.4 ml/m2

OECD SIDS 2006b

- For mid-range chain length category members (C11-C13): low solubility; acute toxicity in the range 0.1-1.0 mg/l,
- Acute effects in fish (96h LC50): from 0.48 mg/l (estimated, C12-14 alcohols) and 0.7-0.8 mg/l (nominal, C6-12 alcohols) to 97 mg/l (measured, Hexanol). No effects up to limit of water solubility for single chain lengths >C13-14 and for some multi-component substances.
- Acute effects in invertebrates (EC50): from 0.13 mg/l (48h estimated, C14-16 alcohols) and 0.8-1.1 mg/l (96 h nominal, 1-undecanol) to 200 mg/l (24h nominal, Hexanol). No effects likely up to the limit of water solubility for single chain lengths >C13 and for some multi-component substances.
- Acute growth rate effects in algae (72 h ErC50): from ca. 0.1 mg/l (nominal, C10-16 and C12-16 alcohols, and estimated for various substances) to 80 mg/l (measured, Hexanol). No effects likely up to the limit of water solubility for single chain lengths >C14 and for some multi-component substances.

- Estimated Data - None

Chronic Aquatic Toxicity (CA): vH

Tetradecanol was assigned a very high with high confidence for chronic aquatic toxicity based on a measured 21-day NOEC of 1.6 µg/L for cumulative number of off-spring of *D. magna* reported for high quality analogs based. Additional studies are available which supports the very high hazard classification. The hazard score is based on results from guideline studies in a high-quality analog and therefore is reported as high confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening:*
    - *Japan - GHS - Hazardous to the aquatic environment (chronic) - Category 1*
    - *German FEA - Substances Hazardous to Waters - Class 2 - Hazard to Waters*
    - *EC - CEPA DSL - Inherently Toxic in the Environment*

- Measured Data

ECHA 2019b

- Reliable EC10 values of 0.43 - >2.4 mg/l and NOEC value of 0.26 mg/l for a range of appropriate endpoints were determined for *Pimephales promelas* exposed to decan-1-ol in a reliable fish early life-stage test. The test was conducted in accordance with GLP and following OECD 210 with appropriate and necessary modifications due to the test substance being a very difficult substance to test. The result is considered definitive.

- A 35 d NOEC value of >140 ug a.i./L has been determined for the effects of the pentadecanol branched on the growth, survival and hatchability of the freshwater fish *Pimephales promelas*. No statistically significant effects were observed at the highest concentration tested. Spine curvature was observed in a few individuals in the treatment vessels.
- A reliable OECD Guideline 211 (*Daphnia magna* Reproduction Test) 21-day $NOEC_{repro}$ value of 14 µg/L was determined for the effects of the test substance on reproduction (cumulative number of offspring) of the freshwater test organism *Daphnia magna*.
- A reliable 21 day reproduction NOEC value of 1.0 mg/L has been determined for the effects of the test substance on reproduction and survival of the freshwater test organism *Daphnia magna.*
- A reliable OECD Guideline 211 (*Daphnia magna* Reproduction Test) 21 d $NOEC_{repro}$ value of 1.6 ug/L has been identified for the effect of the test substance on the cumulative number of off-spring of *D. magna.*

<u>OECD SIDS 2006a</u>

- Toxicity to daphnids: 21-day life-cycle test NOEC = 1.0 mg/l, LOEC (reproduction) = 3.0 mg/lc)
- Toxicity to algae: EC0 = 0.30 mg/l, EC10 = 0.73 mg/l, EC50 = 0.97 mg/l (Senedesmus subspicatus DIN38412, part 9)

<u>OECD SIDS 2006b</u>

- For mid-range chain length category members (C11-C13): low solubility; well-characterized chronic toxicity to aquatic organisms in the range 0.1-<1.0 mg/l;
- Chronic effects in invertebrates: 21-day $NOEC_{repro}$ from 0.0098 mg/l (measured, tetradecanol, based on mean measured initial concentration) to 1 mg/l (measured, octanol). No effects are expected for single chain lengths >C15 up to limit of aqueous solubility.

- Estimated Data - None

ENVIRONMENTAL FATE (FATE)

Persistence (P): vL

Tetradecanol was assigned a very low with high confidence for persistence based on meeting the readily biodegradable 10-day window in most tests conducted under the conditions of OECD Guideline No 301B and 301D. In addition, it is estimated based on high quality analogs that tetradecanol will have a half-life of <2 days if released in air. The hazard score is based on results from guideline studies and are supported by additional results reported for high quality analogs and therefore is reported as high confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data

ECHA 2019a

- OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test). A reliable study conducted according to an appropriate test protocol determined the substance to be readily biodegradable.
- OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test). A ready biodegradation value of 87% was obtained for the test substance using an appropriated test method. The result was considered reliable and meets the 14-day window.
- OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test). Docosan-1-ol was tested for ready biodegradation according to OECD 301B. The degradation of the test item was 87.5 % within 28 days (with reference to the solvent control). The biodegradation of the test item reached the criterion for ready biodegradation.
- A ready biodegradation value of 66% was obtained for the test substance using an appropriate test guideline and in compliance with GLP. Readily biodegradable but failing 10-day window. The result is considered reliable.
- There is very substantial and convincing evidence in support of rapid and complete biodegradation / biotransformation by a range of organisms (bacteria, fungi, algae, fish and mammals) and in a range of environmental media and conditions (particularly aquatic and water/sediment systems) for members of the C6-24 Alcohols category.
- A range of screening and simulation data with different types of cultures is available. The data consistently show that linear and essentially linear aliphatic alcohols in the range C6 - C24 are readily biodegradable in standard screening studies, rapidly and extensively biodegraded under aerobic and anaerobic conditions, biodegradable by garden soil inoculum, biodegraded by algae and aquatic microorganisms in long-term aquatic ecotoxicity tests, and biodegraded in sediments in several studies.
- In accordance with Column 2 of REACH Annex IX, the full soil simulation test (required in Section 9.2.1.3) does not need to be conducted as the substance is readily biodegradable. Furthermore, a close structural analogue, decan-1-ol (CAS 112-30-1), has been shown to be very rapidly degraded in non-sterilized standard soils as part of method development for the soil adsorption study. The data available regarding persistence in soil are limited. A commercial multi-constituent substance (CAS 68155-

00-0 (C14-18 and C16-18 unsaturated) and CAS 68002-94-8 (C16-18 and C18 unsaturated)) was found to be readily biodegradable in a reliable OECD 301D study using a non-standard inoculum; garden soil microorganisms (Borner, 1999).
- The anaerobic biodegradability of a range of chain lengths within the category has been investigated (C6 and C16 alcohols, 2 studies; and C16-18 and C18 unsaturated alcohols, 2 studies). All test substances were anaerobically degradable.

HSDB
- If released to air, a vapor pressure of $8.48X10^{-4}$ mm Hg at 25 deg C indicates 1-dodecanol will exist solely as a vapor in the atmosphere. Vapor-phase 1-dodecanol will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 21 hours.
- 1-Dodecanol does not contain chromophores that absorb at wavelengths >290 nm and, therefore, is not expected to be susceptible to direct photolysis by sunlight.
- If released to soil, 1-dodecanol is expected to have slight mobility based upon Koc values of 2042-3388 in humic acid. Volatilization from moist soil surfaces is expected based upon a estimated Henry's Law constant of $5.19X10^{-5}$ atm-cu m/mole.
- Theoretical BOD values using standard 5-day aerobic sewage tests ranged from 20-29.7% indicate that biodegradation may be an important environmental fate process in soil and water. If released into water, 1-dodecanol is expected to adsorb to suspended solids and sediment based upon a Koc of 7700 measured in suspended solids. Volatilization from water surfaces is expected based upon this compound's Henry's Law constant.
- Estimated volatilization half-lives for a model river and model lake are 27 hours and 12 days, respectively. However, volatilization from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. The volatilization half-life from a model pond is about 11 months when adsorption is considered. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions (pH 5 to 9).
- A 5-day theoretical BOD of 20% was observed for 1-dodecanol in an aerobic screening test using a sewage inoculum. A 5-day theoretical BOD of 23.2% was observed for 1-dodecanol in a standard BOD dilution test using a mixed microbial inoculum. A 5-day theoretical BOD of 27-29.7% was observed for 1-dodecanol in a standard BOD aerobic screening test using a sewage inoculum or an acclimated activated sludge inoculum; using a Warburg respirometer technique and a sewage inoculum, a 6-hr theoretical BOD of 15.2% was observed. Using a Warburg respirometer technique and various activated sludge inoculum, respective 6-hr, 12-hr and 24-hr theoretical BODs of 4.5, 10.1 and 13.4% were observed. 1-Dodecanol was found to be readily biodegraded.
- Estimated Data

OECD SIDS 2006b
- The Mackay I model predicts initial partitioning to air and soil/sediments (Air 67.43%, Water 1.51%, soil 16.07% and sediment 15.00%). In fact, some volatization from open water can be expected. The exact vapor pressure is however, critical for this chemical in the Mackay model, and long-term models (such as Neely 100-day) indicate that binding to sediments will limit the amount lost to volatization.
- Predicted data from the SRC BIOWIN v4.10 program (part of the EPIWeb suite v4.01) supports rapid degradation for the linear alcohols, but cannot be used quantitatively. However, the extent of measured data means that it is not necessary to rely upon any

form of (Q)SAR: interpolation to fit data gaps can be done by expert judgement across the data set.
- It is important for context to note the findings from studies in the EU and US which consistently show that anthropogenic alcohols in the environment are minimal compared to the level of natural occurrence. Using stable isotope signatures of fatty alcohols in a wide variety of household products and in environmental matrices sampled from river catchments in the United States and United Kingdom, Mudgeet al.(2012) estimated that 1% or less of fatty alcohols in rivers are from waste water treatment plant (WWTP) effluents, 15% is from in situ production (by algae and bacteria), and 84% is of terrestrial origin. Further, the fatty alcohols discharged from the WWTP are not the original fatty alcohols found in the influent. While the compounds might have the same chain lengths, they have different stable isotopic signatures (Mudgeet al., 2012).

Bioaccumulation (B): *M*

Tetradecanol was assigned a moderate with low confidence for bioaccumulation based on estimated BCF for long chain aliphatic alcohols values that fall within the >500 to 1000 range. While the reported Log Kow value indicates a higher bioaccumulation potential, this value will overestimate BCF because they take no account of biotransformation and metabolism of alcohols by a wide range of biota from bacteria to mammals. Specifically, alcohols are metabolized/biotransformed in living organisms; this biotransformation suggests that bioaccumulation potentials based on octanol-water partition coefficients may be overestimates. Measured BCF data on a related alcohols category supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log Kow. The hazard score is based on an estimated BCF/BAF and therefore is reported as lower confidence.

Data
- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data
  ECHA 2019a
  - The test substance was observed to undergo extensive metabolism in fish after force-feeding for 72 h, the result is considered reliable.
  - A log n-octanol/water partition coefficient of 5.5 was determined for tetradecan-1-ol in accordance with ASTM E 1147. The result is considered to be reliable.
- Estimated Data
  ECHA 2019a
  - All the reviewed data indicate that log Kow-based QSARs overestimate BCF because they take no account of biotransformation and metabolism of alcohols by a wide range of biota from bacteria to mammals. These observations have recently been critically assessed using cellular biotransformation assays of ethoxylated alcohols and other aliphatic surfactants which confirm that metabolism of the alkyl chain can lower BCF by orders of magnitude. For the more soluble chain lengths, evaluated in non-guideline BCF studies on linear alcohols and guideline studies for

branched alcohols, predicted BCFs are overestimated by at least an order of magnitude.

- For the multi-constituent/UVCB long chain alcohols, a single BCF value is difficult to predict. However, the values for the constituents present are relevant. There is ample experimental in vivo evidence of metabolism in various trophic levels. Rapid biotransformation into tissue lipids has been demonstrated in fish (carp), for oleyl alcohol (C18, unsaturated). Biotransformation of linear structures has been demonstrated to be faster than for multiply-branched structures in accordance with expectations based upon the metabolic pathways. Predicted bioconcentration factors, using methods which take account of the expected metabolism in vivo, estimate low BCF values. Experimental studies using structural analogues show low BCF values. All linear alcohols in this chain length range are readily biodegradable in reliable standard studies.
- BCF can be calculated using EPI BCFBAF v3.01 (2012). This model uses a log Kow-based equation with modified algorithms for specific structural features. This version of the software also incorporates for the first time a modification for biotransformation in vivo. These considerations suggest that it is unlikely that bioaccumulation would be exhibited in nature for alcohols in the C6-24 linear and essentially-linear alcohols category.
- It is therefore concluded that the long-chain alcohols in this category are non-bioaccumulative. This conclusion is considered to be sufficiently well-supported to justify no need for further testing in fish, since vertebrate testing for the purposes of REACH registration should be avoided where adequate existing evidence exists, and in view of the expected severe technical difficulties in conducting such a test.

ECHA 2019b

- The test substance was observed to undergo extensive metabolism in fish after force-feeding for 72 h, the result is considered reliable.
- A BCF value of BCF = 47.6 L/kg wet-wt and BAF = 445 L/kg wet-wt calculated using SRC BCFBAF v3.01 (2012).
- An estimated BCF value of 3801 L/kg has been reported for dodecan-1-ol from the Danish Environmental Protection Agency in 1993 which is considerably higher than the modelled result using the BCFBAF QSAR model. As no guideline was followed and no other information is reported, this value is considered outdated and therefore the study is disregarded.
- A BCF value of 26 was obtained using an accepted calculation method. The result is considered to be reliable.
- All the reviewed data indicate that log Kow-based QSARs overestimate BCF because they take no account of biotransformation and metabolism of alcohols by a wide range of biota from bacteria to mammals (Veenstraet al., 2009; Mudge, 2008). These observations have recently been critically assessed using cellular biotransformation assays of ethoxylated alcohols and other aliphatic surfactants which confirm that metabolism of the alkyl chain can lower BCF by orders of magnitude (Dyeret al., 2008; Cowan-Ellsberryet al., 2008). For the more soluble chain lengths, evaluated in non-guideline BCF studies on linear alcohols and guideline studies for branched alcohols, predicted BCFs are overestimated by at least an order of magnitude.

HSDB

- An estimated BCF of 48(SRC), from its log Kow of 5.13 and a regression-derived equation, suggests the potential for bioconcentration in aquatic organisms is moderate.

OECD SIDS 2006b

- No reliable guideline-standard measured bioconcentration data are available. Bioconcentration factors (BCF) calculated on the basis of log Kow range from 7.0 for C6 to a maximum of 46000 for C16, reducing to 1100 for C22. For hexadecanol, the BCF (Q)SAR estimates a value of 45300 (recalculated from the parabolic Connell and Hawker equation), but a measured value of 56 and a range of values from 507-1550 from two unreliable studies exist; BCF data for alcohols similar to those in this family but with 2.1-2.9 branches per molecule also indicate that BCF (Q)SAR overestimate BCF. Log Kow-based BCF (Q)SAR predictions also take no account of biotransformation/metabolism of alcohols in living organisms, the natural mechanism for their removal. For these reasons it is expected that category member s will have a low potential for bioaccumulation.
- Measured BCF data on a related alcohols Category supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log Kow
- Alcohols are metabolized/biotransformed in living organisms; this biotransformation suggests that bioaccumulation potentials based on octanol-water partition coefficients may be overestimates. Measured BCF data on a related alcohols Category supports the concept that the bioaccumulation potential of these substances will be lower than estimated from log Kow.

EPISUITE

- Log BCF Arnot-Gobas method (upper trophic) = 2.724 (BCF = 529.8)
- Log BAF Arnot-Gobas method (upper trophic) = 2.737 (BAF = 546.2)

PHYSICAL HAZARDS (PHYSICAL)

Reactivity (Rx): *L*

Tetradecanol was assigned a low with low confidence for reactivity based on the absence of chemical groups that are associated with explosivity or oxidizing properties. The reactivity endpoints reported for Tetradecanol are not directly comparable to the hazard breaks within GreenScreen and therefore professional judgement has been used in determining the low hazard score. The hazard score is based on professional judgement using the available data and is reported as low confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*

- Measured Data

- Estimated Data

  ECHA 2019a
  - The molecule has no chemical groups that are associated with explosive properties. Therefore, in accordance with Column 2 of REACH Annex VII, there is no need to conduct the explosive properties study.
  - On the basis of structure, the substance is expected to be incapable of reacting exothermically with combustible materials. Therefore, in accordance with Column 2 of REACH Annex VII, there is no need to conduct the oxidizing properties study.

  PubChem 2019
  - Instability: 0. 0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water.

Flammability (F): L

Tetradecanol was assigned a rating of low with High confidence for flammability based on a flash point of 155°C and boiling point of 294°C. Therefore, this substance is not classified as flammable based on the GHS criteria. The hazard score is based on measured data and is therefore reported as high confidence.

Data

- Lists
  - *Authoritative: not included on any authoritative lists*
  - *Screening: not included on any screening lists*
  - *:*
- Measured Data

  ECHA 2019a
  - The substance is not classified for flammability in accordance with Regulation (EC) No. 1272/2008. This is on the basis of a measured flash point of 155°C and boiling point of 294°C.

- No ignition observed over a 5 -minute period (ambient temperature 20ºC)
- An auto-ignition temperature value of 259°C at 1013 hPa was determined in accordance with ASTM E 659. The result is considered to be reliable and is selected as key study.

- Estimated Data - None

REFERENCES

ECHA 2019a. European Chemicals Agency Registered Substance Database. Tetradecanol. Available at https://echa.europa.eu/registration-dossier/-/registered-dossier/15422/1

ECHA 2019b. European Chemicals Agency Registered Substance Database. 1-Dodecanol. Available at https://echa.europa.eu/registration-dossier/-/registered-dossier/15424/1

HSDB. Hazardous Substance Database. 1-Dodecanol (CAS# 112-53-8). Toxicology Data Network. Available at < https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+1075>

MAK Value Documentation, 2006. 1-dodecanol. Available at https://onlinelibrary.wiley.com/doi/full/10.1002/3527600418.mb11253kske0022

Mudge, S. 2005. Fatty Alcohols – a review of their natural synthesis and environmental distribution. Executive Summary of the Soap and Detergent Association.

OECD SIDS 2006a. SIDS Initial Assessment Profile. 1-Dodecanol. Available at https://hpvchemicals.oecd.org/UI/handler.axd?id=f19767ea-a6c2-4300-8763-038aa7dd0037

OECD SIDS 2006b. SIDS Initial Assessment Profile. Long Chain Alcohols. Available at http://www.aciscience.org/docs/Draft_SIDS_Long_Chain_Alcohols_1.pdf

Pubchem 2019. National Center for Biotechnology Information. PubChem Compound Database; CID=8193, https://pubchem.ncbi.nlm.nih.gov/compound/8193 (accessed Feb. 11, 2019). Available at https://pubchem.ncbi.nlm.nih.gov/compound/1-dodecanol#section=Top

APPENDIX A: HAZARD CLASSIFICATION ACRONYMS

(alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

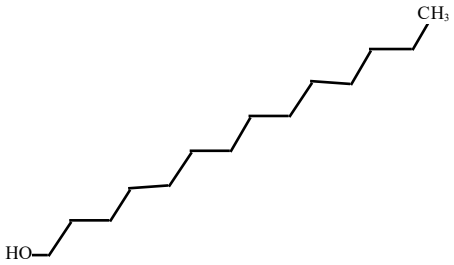
(ST) Systemic/Organ Toxicity

APPENDIX B – MODELING RESULTS

Attach:

- **EPISuite Results for 1-Tetradecanol (CASRN 112-72-1)**

EPI Suite Results For CAS 112-72-1




```
SMILES : OCCCCCCCCCCCCCC
CHEM   : 1-Tetradecanol
MOL FOR: C14 H30 O1
MOL WT : 214.39
------------------------------ EPI SUMMARY (v4.11) --------------------------
Physical Property Inputs:
Log Kow (octanol-water):   5.50
Boiling Point (deg C)  :   ------
Melting Point (deg C)  :   ------
Vapor Pressure (mm Hg) :   ------
Water Solubility (mg/L):   ------
Henry LC (atm-m3/mole) :   ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.68 estimate) =  5.75
Log Kow (Exper. database match) =  6.03
Exper. Ref:  BURKHARD,LP ET AL. (1985B)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C):  303.68  (Adapted Stein & Brown method)
Melting Pt (deg C):  49.43  (Mean or Weighted MP)
VP(mm Hg,25 deg C):  0.000201  (Modified Grain method)
VP (Pa, 25 deg C) :  0.0269  (Modified Grain method)
MP  (exp database):  39.5 deg C
BP  (exp database):  289 deg C
```

```
VP  (exp database):  1.10E-04 mm Hg (1.47E-002 Pa) at 25 deg C
Subcooled liquid VP: 0.000153 mm Hg (25 deg C, exp database VP )
: 0.0204 Pa  (25 deg C, exp database VP )

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L):  2.396
log Kow used: 5.50 (user entered)
no-melting pt equation used
Water Sol (Exper. database match) =  0.191 mg/L (25 deg C)
Exper. Ref:  YALKOWSKY,SH & HE,Y (2003)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) =  0.7571 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method :   1.70E-004  atm-m3/mole  (1.72E+001 Pa-m3/mole)
Group Method:   3.08E-004  atm-m3/mole  (3.12E+001 Pa-m3/mole)
Exper Database: 1.60E-04  atm-m3/mole  (1.62E+001 Pa-m3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC:  not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC:  2.366E-005 atm-m3/mole  (2.398E+000 Pa-m3/mole)
VP:   0.000201 mm Hg (source: MPBPVP)
WS:   2.4 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used:  5.50  (user entered)
Log Kaw used:  -2.184  (exp database)
Log Koa (KOAWIN v1.10 estimate):  7.684
Log Koa (experimental database):  None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model)         :   0.9126
Biowin2 (Non-Linear Model)     :   0.9491
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model):   3.1837  (weeks       )
Biowin4 (Primary Survey Model) :   3.9369  (days        )
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model)    :   0.8783
Biowin6 (MITI Non-Linear Model):   0.9499
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model):  0.9094
Ready Biodegradability Prediction:   YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled):  0.0204 Pa (0.000153 mm Hg)
Log Koa (Koawin est  ): 7.684
Kp (particle/gas partition coef. (m3/ug)):
Mackay model           :  0.000147
Octanol/air (Koa) model:  1.19E-005
```

```
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model     :  0.00528
Mackay model           :  0.0116
Octanol/air (Koa) model:  0.000948

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant =  21.0205 E-12 cm3/molecule-sec
Half-Life =     0.509 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life =     6.106 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
0.00846 (Junge-Pankow, Mackay avg)
0.000948 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc    :  1403  L/kg (MCI method)
Log Koc:  3.147       (MCI method)
Koc    :  3596  L/kg (Kow method)
Log Koc:  3.556       (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 1.922 (BCF = 83.48 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 0.1356 days (HL = 1.367 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.724 (BCF = 529.8)
Log BAF Arnot-Gobas method (upper trophic) = 2.737 (BAF = 546.2)
log Kow used: 5.50 (user entered)

Volatilization from Water:
Henry LC:  0.00016 atm-m3/mole  (Henry experimental database)
Half-Life from Model River:      6.852  hours
Half-Life from Model Lake :      197.5  hours   (8.23 days)

Removal In Wastewater Treatment:
Total removal:              88.40  percent
Total biodegradation:        0.74  percent
Total sludge adsorption:    87.18  percent
Total to Air:                0.48  percent
(using 10000 hr Bio P,A,S)

Removal In Wastewater Treatment (recommended maximum 95%):
Total removal:              99.97  percent
Total biodegradation:       78.81  percent
Total sludge adsorption:    21.14  percent
Total to Air:                0.02  percent
(using Biowin/EPA draft method)

Level III Fugacity Model:
Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       1.46           12.2         1000
Water     19.9           360          1000
```

```
Soil      77.7            720          1000
Sediment  0.933           3.24e+003    0
Persistence Time: 434 hr
```

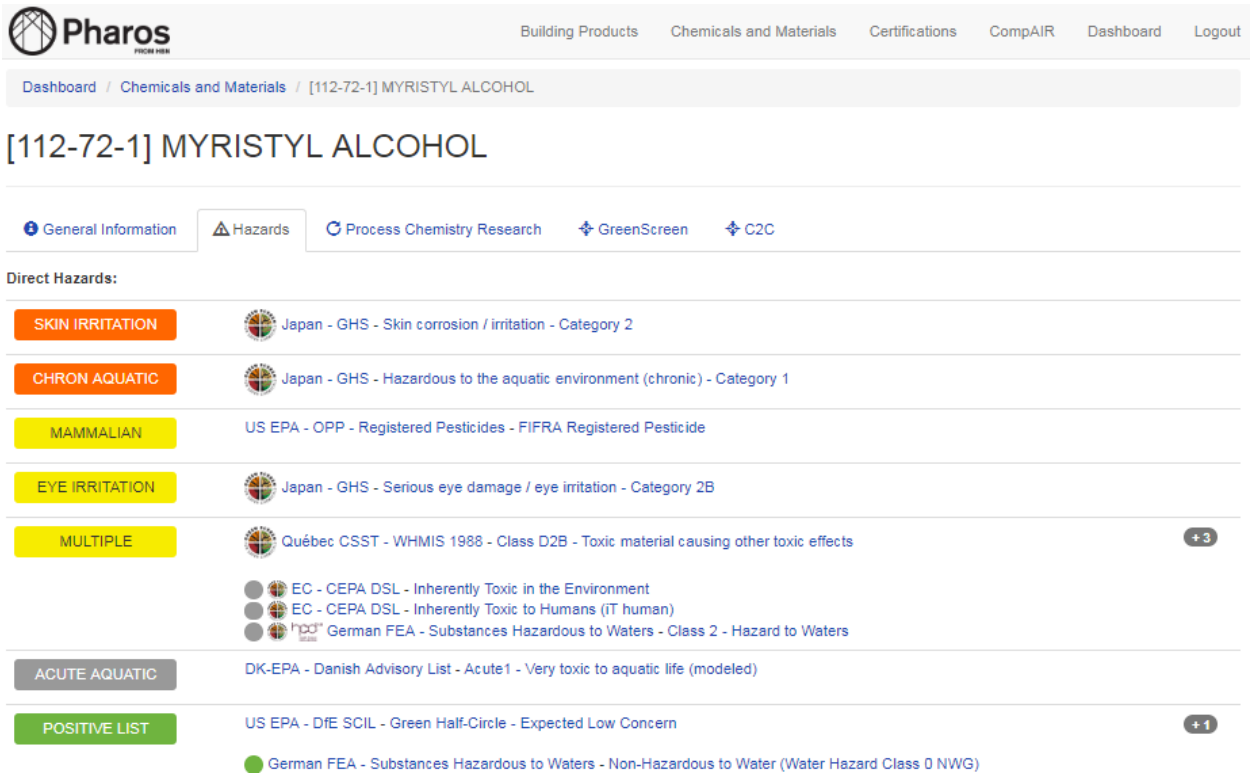
- **ECOSAR Results for 1-Tetradecanol (CASRN 112-72-1)**

```
ECOSAR Program (v1.11) Results:
==============================
ECOSAR Version 1.11 Results Page

SMILES : OCCCCCCCCCCCCCC
CHEM   : 1-Tetradecanol
CAS Num: 112-72-1
ChemID1:
MOL FOR: C14 H30 O1
MOL WT : 214.39
Log Kow: 5.752      (EPISuite Kowwin v1.68 Estimate)
Log Kow:            (User Entered)
Log Kow: 6.03       (PhysProp DB exp value - for comparison only)
Melt Pt:            (User Entered for Wat Sol estimate)
Melt Pt: 39.50      (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 0.7125     (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol:            (User Entered)
Wat Sol: 0.191      (mg/L, PhysProp DB exp value)


-------------------------------------
Values used to Generate ECOSAR Profile
-------------------------------------
Log Kow: 5.752      (EPISuite Kowwin v1.68 Estimate)
Wat Sol: 0.191      (mg/L, PhysProp DB exp value)



-------------------------------------
ECOSAR v1.11 Class-specific Estimations
-------------------------------------
Neutral Organics
Predicted
ECOSAR Class                 Organism            Duration  End Pt   mg/L
(ppm)
==========================  ==================  ========  ======
==========
Neutral Organics           : Fish                96-hr     LC50        0.075
Neutral Organics           : Daphnid             48-hr     LC50        0.060
Neutral Organics           : Green Algae         96-hr     EC50        0.188
Neutral Organics           : Fish                          ChV         0.011
Neutral Organics           : Daphnid                       ChV         0.015
Neutral Organics           : Green Algae                   ChV         0.107
Neutral Organics           : Fish (SW)           96-hr     LC50        0.097
Neutral Organics           : Mysid               96-hr     LC50        0.006
Neutral Organics           : Fish (SW)                     ChV         0.104
Neutral Organics           : Mysid (SW)                    ChV      0.000161
```

```
Neutral Organics           : Earthworm           14-day    LC50      152.171
*

Note:  * = asterisk designates: Chemical may not be soluble enough to
measure this predicted effect. If the effect level exceeds the
water solubility by 10X, typically no effects at saturation (NES)
are reported.


------------------------------
Class Specific LogKow Cut-Offs
------------------------------
If the log Kow of the chemical is greater than the endpoint specific cut-offs
presented below, then no effects at saturation are expected for those
endpoints.

Neutral Organics:
----------------
Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogKow: 6.0 (Earthworm LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
```

- **Other**

APPENDIX C – PHAROS OUTPUT FOR Tetradecanol (CAS# 112-72-1)]



APPENDIX D – USE OF THE ASSESSMENT

When making reference to this GreenScreen assessment, users shall include the following note:

> The publicly available, certified GreenScreen Assessment for Tetradecanol (CAS# 112-72-1) was prepared by WAP Sustainability Consulting, LLC on May 13th, 2019, expiring May 13th, 2024, the details of which can be found at http://www.wapsustainability.com/greenscreen-for-safer-chemicals.

This reference shall be used when the final GreenScreen benchmark score is shown without access to this full assessment report, including, but not limited to, Health Product Declarations (HPDs) and manufacturer's inventories for LEED documentation.