Dodecyldimethylamine Oxide (1643-20-5) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared by:

ToxServices LLC

June 6, 2016

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING
1367 Connecticut Ave., N.W., Suite 300
Washington, D.C. 20036

TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Dodecyldimethylamine Oxide (1643-20-5)

Dodecyldimethylamine oxide is an alkyldimethylamine oxide that functions as a foam booster and stabilizer; as a foam builder and stabilizer, viscosity enhancer, emollient, conditioner, emulsifier, antistatic agent, and wetting agent in cosmetic formulations; as a component of dishwasher detergents, shampoos, soaps and antiaging products; as an antifungal and antibacterial agent; and, at industrial sites, used for the transfer of substances, roller applications, and as a laboratory reagent.

Dodecyldimethylamine oxide was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes"). This score is based on the following hazard score combinations:

- Benchmark 2e ("Moderate T (Group I Human)")
  - Moderate Group I Human Health Hazard (reproductive toxicity (R) and developmental toxicity (D))
- Benchmark 2f ("Very High T (Ecotoxicity or Group II Human) or High T (Group II* Human)")
  - Very High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))
  - Very High Group II Human Health Hazard (single dose neurotoxicity (Ns), skin irritation (IrS), and eye irritation (IrE))

Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in GreenScreen® Guidance Section 11.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), dodecyldimethylamine oxide meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if dodecyldimethylamine oxide were assigned a High score for the data gap endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:

As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal, and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for Dodecyldimethylamine Oxide

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	**L**	*M*	*M*	DG	**M**	*H*	*M*	*vH*	*M*	**L**	DG	*vH*	**vH**	**vH**	**vH**	**vL**	*vL*	*L*	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they 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. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Assessment for Dodecyldimethylamine Oxide (1643-20-5)

Method Version: GreenScreen® Version 1.3[1]
Assessment Type[2]: Certified
Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment Prepared By:
Name: Zach Guerrette, Ph.D., D.A.B.T.
Title: Toxicologist
Organization: ToxServices LLC
Date: June 2, 2016

Quality Control Performed By:
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Toxicologist
Organization: ToxServices LLC
Date: June 6, 2016

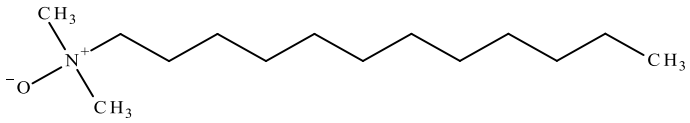
Confirm application of the *Disclosure and Assessment Rules and Best Practice*[3]: (List disclosure threshold and any deviations) Amine oxides such as dodecyldimethylamine oxide do not exist as pure substances, but rather are manufactured, transported and used in aqueous solutions. Typically the aqueous solutions have concentrations of 25 – 35%. Impurities may exist such as hydrogen peroxide present at trace levels and free amine (<1%) (OECD 2006). According to GreenScreen Guidance (CPA 2016a), a full GreenScreen® assessment is required for each impurity present at 100 ppm and above and every intentional ingredients, while a list translator screening is required for impurities present at < 100 ppm. This screen was performed on generic dodecyldimethylamine oxide, and therefore no specific impurity information is available.

Notes related to production specific attributes[4]:
Trace levels of stabilizers, processing aids or other impurities may be present depending on the method of production. As this screen is performed on generic dodecyldimethylamine oxide, no manufacturer-specific information is available.

Chemical Name: Dodecyldimethylamine Oxide

CAS Number: 1643-20-5

Chemical Structure(s):



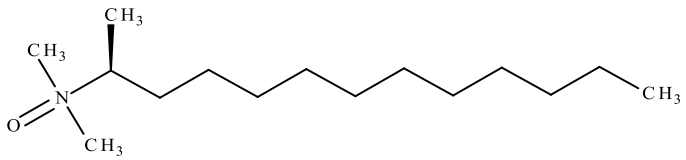
Also called: 1-Dodecanamine, N,N-dimethyl-, N-oxide; Lauramine oxide; Lauryl dimethyl amine oxide; N,N-Dimethyl-1-dodecanamine-N-oxide; 1-Dodecanamine, N,N-dimethl-, N-oxide; DDNO;

[1] Use GreenScreen® Hazard Assessment Guidance (Guidance) v1.3
[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen® Verification Program)
[3] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

[4] Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.

Dimethylaurylamine oxide; Dimethyldodecylamine N-oxide; Dimethyldodecylamine oxide; Dimethyllaurylamine oxide; Dodecylamine, N,N-dimethyl-, N-oxide; Dodecyldimethylamine N-oxide; EC 216-700-6; Lauryldimethylamine N-oxide; Lauryldimethylamine oxide; N,N-Dimethyldodecylamine oxide; n-Dodecyldimethylamine oxide; N-Lauryl-N,N-dimethylamine oxide; N-Lauryldimethylamine N-oxide (ChemIDplus 2016)

Suitable analogs or moieties of chemicals used in this assessment (CAS #'s):
For the mutagenicity endpoint, no clastogenicity tests were identified for dodecyldimethylamine oxide. Therefore, data for N,N-dimethyl-1-methyldodecylamine oxide (CAS #60729-78-4) were used to address this data gap. ToxServices considered N,N-dimethyl-1-methyldodecylamine oxide to be a suitable analog for dodecyldimethylamine oxide as their chemical structures differ by the presence of one methyl group on the alkyl chain.



Analog: N,N-Dimethyl-1-methyldodecylamine oxide (CAS #60729-78-4)

Additionally, data were identified for amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6) and amines, C10-16-alkyldimethyl, N-oxides (CAS #70592-80-2). Dodecyldimethylamine oxide is a C12 dimethylamine oxide. Therefore, data for amines, C12-14 (even numbered)-alkyldimethyl, N-oxides and amines, C10-16-alkyldimethyl, N-oxides were included this assessment. No structures were identified for these two surrogates as they are mixtures.

Identify Applications/Functional Uses (HSDB 2009, ECHA 2016; use levels not specified)**:**
1. Foam booster and stabilizer;
2. Foam builder and stabilizer, viscosity enhancer, emollient, conditioner, emulsifier, antistatic agent, and wetting agent in cosmetic formulations;
3. Component of dishwasher detergents, shampoos, soaps and antiaging products;
4. Antifungal and antibacterial agent
5. At industrial sites: used for the transfer of substances, roller applications, and as a laboratory reagent.

GreenScreen® Summary Rating for Dodecyldimethylamine Oxide[5,6 7,8]**:** Dodecyldimethylamine oxide was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2016c). This score is based on the following hazard score combinations:

- Benchmark 2e ("Moderate T (Group I Human)")
    - Moderate Group I Human Health Hazard (reproductive toxicity (R) and developmental toxicity (D))

[5] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[6] See Appendix A for a glossary of hazard endpoint acronyms
[7] For inorganic chemicals only, see GreenScreen Guidance v1.3 Section 13. (Exceptions for Persistence)
[8] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen Guidance v1.3 Section 8.2.1.

- Benchmark 2f ("Very High T (Ecotoxicity or Group II Human) or High T (Group II* Human)")
  - Very High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))
  - Very High Group II Human Health Hazard (single dose neurotoxicity (Ns), skin irritation (IrS), and eye irritation (IrE))

Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in GreenScreen® Guidance (CPA 2016a) Section 11.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), dodecyldimethylamine oxide meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if dodecyldimethylamine oxide were assigned a High score for the data gap endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Dodecyldimethylamine Oxide

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	**L**	*M*	*M*	DG	**M**	*H*	*M*	*vH*	*M*	**L**	DG	*vH*	**vH**	**vH**	**vH**	**vL**	*vL*	*L*	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they 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. Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings[9]:

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[10]

No transformation products were identified for dodecyldimethylamine oxide. Hydrolysis of dodecyldimethylamine oxide is not expected as it lacks functional groups that undergo hydrolysis under environmental conditions (HSDB 2009). A GLP-compliant hydrolysis test conducted according to OECD TG 111 was performed with the analog amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (purity not specified) using a concentration of 4.167 mg/L, and a pH of 4, 7, or 9 at 50°C for 5 days. Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was deemed to be hydrolytically stable in this test as the total recovery exceeded 93% under the tested conditions. In addition, reliable biodegradation studies on dodecyldimethylamine oxide indicate that it meets the 10-day window in ready biodegradability tests. Therefore, it is not expected to form any degradation products persistent enough to be relevant for this assessment. ToxServices concludes that dodecyldimethylamine oxide is stable in the environment and that the Benchmark Score for dodecyldimethylamine oxide is not modified by transformation products.

[9] See GreenScreen Guidance v1.3 Section 12.
[10] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

Introduction

Dodecyldimethylamine oxide is used as a foam booster and stabilizer; as a foam builder and stabilizer, viscosity enhancer, emollient, conditioner, emulsifier, antistatic agent, and wetting agent in cosmetic formulations; as a component of dishwasher detergents, shampoos, soaps and antiaging products; and as an antifungal and antibacterial agent (HSDB 2009). At industrial sites, this chemical is used for the transfer of substances, roller applications, and as a laboratory reagent (ECHA 2016). No use levels were specified for any of these functions. Dodecyldimethylamine oxide is produced via the reaction of dimethyl-N-dodecylamine (CAS #112-18-5) with hydrogen peroxide (CAS #7722-84-1) (HSDB 2009).

ToxServices assessed dodecyldimethylamine oxide against GreenScreen® Version 1.3 (CPA 2016a) following procedures outlined in ToxServices' SOPs 1.37 and 1.69 (GreenScreen® Hazard Assessment) (ToxServices 2013a,b).

U.S. EPA Safer Choice Program's Safer Chemical Ingredients List (SCIL)

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2016). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015).

Dodecyldimethylamine oxide is present on the Safer Choice SCIL as a surfactant with a full green circle meaning that it has been verified to be of low concern based on experimental and modeled data.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2016a.b). Pharos (Pharos 2016) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b)[11] and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for dodecyldimethylamine oxide can be found in Appendix C and a summary of the results can be found below:

- Very High Hazard
  - Acute Aquatic Toxicity
    - Japan GHS: Hazardous to the aquatic environment (acute) – Category 1
- High Hazard
  - Eye Irritation
    - New Zealand GHS – 8.3A (GHS Category 1): Corrosive to ocular tissue
    - Japan GHS: Serious eye damage/eye irritation – Category 2A
  - Skin Irritation
    - New Zealand GHS – 8.2B (GHS Category 1): Corrosive to dermal tissue
  - Acute Aquatic Toxicity
    - New Zealand GHS – 9.1A (fish) (GHS Category 1): Very ecotoxic in the aquatic environment
- Medium Hazard
  - Skin Irritation
    - Japan GHS - Skin corrosion / irritation - Category 2

[11] DOT lists are not required lists for GreenScreen List Translator v1.3. They are reference lists only.

- Dodecyldimethylamine oxide is listed as a severe marine pollutant in Appendix B of U.S. DOT (2008a). It is not listed in U.S. DOT (2008b).

Physicochemical Properties of Dodecyldimethylamine Oxide

Dodecyldimethylamine oxide is a white powdery solid under standard temperature and pressure. It has a low vapor pressure (6.23×10^{-8} mmHg) indicating that it exists mostly in the solid phase. It is very soluble in water (190,000 mg/L) but is predicted to be more soluble in octanol than in water (log K_{ow} = 1.85). Its log K_{ow} value indicates that it is not likely to bioaccumulate in aquatic biota based on the GreenScreen® criteria for bioaccumulation. Dodecyldimethylamine oxide is not an ethoxylated or propoxylated surfactant. No preservative was identified for this chemical. The dissociation constant being less than 7 indicates that dodecyldimethylamine oxide will exist in its ionic form in naturally-occurring bodies of water and in biological fluids.

Table 1: Physical and Chemical Properties of Dodecyldimethylamine Oxide (1643-20-5)

Property	Value	Reference
Molecular formula	C14-H31-N-O	ChemIDplus 2016
SMILES Notation	C(CCCCCCCCC)CC[N+](C)(C)[O-]	ChemIDplus 2016
Molecular weight	229.405 g/mol	ChemIDplus 2016
Physical state	Solid	ECHA 2016
Appearance	White powder	ECHA 2016
Melting point	132-133°C 130-134°C	ChemIDplus 2016 ECHA 2016
Vapor pressure	6.23×10^{-8} mmHg at 25°C (estimated) 2.1×10^{-5} Pa (1.58×10^{-7} mm Hg) at 25°C	ChemIDplus 2016 ECHA 2016
Water solubility	190,000 mg/L at 25°C 409,500 mg/L[a]	ChemIDplus 2016 ECHA 2016
Dissociation constant	pKa = 4.05 between 25-26.9°C (OECD TG 112)[a]	ECHA 2016
Density/specific gravity	Relative density = 0.983 at 23°C (OECD TG 109)	ECHA 2016
Partition coefficient	Log K_{ow} = 1.85 (estimated from measured solubility in octanol and the critical micelle concentration in water)[a]	ECHA 2016
Supplier, Tradename(s)	N/A	N/A
Ethoxylated or propoxylated?	No	N/A
1,4-Dioxane level	N/A	N/A
# EO Units	N/A	N/A
# PO Units	N/A	N/A
EO/PO Ratio	N/A	N/A
Identity and concentration of preservatives	N/A	N/A

a. Values are for the analog amines, C12-14(even numbered)-alkyldimethyl, N-oxides (CAS #NA, EC #931-292-6)

Toxicokinetics

- ECHA 2016
  - A pre-GLP-compliant toxicokinetics study was performed with Sprague-Dawley rats (2/sex/dose group) provided diets containing ^{14}C-labeled dodecyldimethylamine oxide (10

µCi/g) at 0.5% for 1 or 10 days (2 groups each). The animals were subsequently provided non-radioactive diet. Urine was collected at 24-hour intervals beginning after the first dose. Other tissues were collected at sacrifice. Blood concentrations of the radiolabeled material ranged from 3-6 µg/g following the single-day dose and 31-50 µg/g following the 10-day dosing. Radioactivity levels in tissues were similar or less than the blood concentrations with the exception of the liver, kidney, and adrenal glands which were greater. One group of male rats administered the 1-day dose also had radioactivity levels in the pancreas and hearts that were greater than the blood levels. Females administered the 10-day dose exhibited higher radioactivity levels in the uterine and body fat and pancreas relative to the blood levels. Following the 10-day dosing, females excreted a smaller portion of the radioactivity into the urine compared to males (37.1% compared to 46.8%). Sex-related differences were observed in the metabolites measured in the urine for one of the groups administered the 1-day dose and both groups administered the 10-day dosing: females excreted more of one metabolite relative to a second metabolite (neither identified but labeled metabolite E and D, respectively), while males excreted more of metabolite D than E in the urine. Metabolites D and E, taken together, accounted for approximately 10% more of the urinary radioactivity in males relative to females (33% vs. 23%).

- A non-GLP-compliant toxicokinetics study conducted in a manner similar to OECD TG 417 was performed with New Zealand rabbits (2/sex/dose group) administered single oral doses of ^{14}C-labeled dodecyldimethylamine oxide (10 µCi/g) in water at 1 mg/kg. The maximum blood concentration of radioactivity was reached approximately 1.5 hours after dosing. The majority of metabolite peaks observed in the plasma were also observed in the urine. Most of the radioactivity was eliminated in the urine, with approximately 30% being eliminated as CO_2 and less than 10% eliminated via the feces. No sex-related differences were observed in the elimination pattern. A total of 10 urinary metabolites were isolated and identified. The primary metabolites were N,N-dimethyl-N-oxide-4-aminobutyric acid and N,N-dimethyl-4-aminobutyric acid which represent 33 and 24% of the eliminated radioactivity, respectively.
- A pre-GLP toxicokinetics study was performed with human volunteers (2 total) administered single oral doses of ^{14}C-labeled dodecyldimethylamine oxide (greater than 98.5% purity) in water at 50 mg (100 µCi). Urine and carbon dioxide samples were collected for up to 144 hours and 72 hours, respectively. The highest concentration of radioactivity in blood samples was measured 1 hour after dosing, indicative of rapid absorption. Excretion was also rapid as 50% and 37% of the administered radioactivity was measured in the urine within 24 hours of dosing. Expired CO_2 collected in the 24 hours after dosing contained 18% and 22% of the administered radioactivity. Comparatively, only 2.7% and 2.5% of the radioactivity was measured in the feces. A total of 79.8% and 69.3% of the radioactivity was recovered.
- A pre-GLP toxicokinetics study conducted according to OECD TG 417 was performed with rats (strain not specified, 4/sex/dose group) administered single oral doses of ^{14}C-labeled dodecyldimethylamine oxide (greater than 98.5% purity, 1 µCi/g) at 100 mg for intra-gastric administration via gavage or 40 mg via stomach intubation for a bile duct experiment. Extensive and rapid absorption was observed (no further details provided). The greatest accumulation and the highest concentration of radioactivity were observed in the liver, with 1.48% of the administered radioactivity measured there. No sex-related differences in the distribution of radioactivity were observed. Maximum radioactivity levels in the liver, kidney, and blood were reached within one hour of dosing. Within 24 hours of dosing, 67.4% of the administered radioactivity was excreted in male rats. Of the radioactivity expired as ^{14}C-radiolabeled CO_2, more than two-thirds appeared in the exhaled breath within

12 hours of dosing. Approximately 9.4% of the administered dose was excreted via the feces. The biliary pathway was identified as a minor excretory pathway for dodecyldimethylamine oxide.

- A pre-GLP toxicokinetics study was performed with human volunteers (2 total) administered dermal doses of ^{14}C-radiolabled dodecyldimethylamine oxide (greater than 98.5% purity) in water at 10 mg (100 µCi). Dermal absorption of the radiolabeled material was limited, as only 0.01% and 0.23% of the radioactivity was measured in the excretion products. More than 92% of the administered dose could be recovered from the site of application. The stratum corneum contained less than 0.2% of the applied dose. All blood samples collected contained less than 0.00003% of the dose per gram.
- A pre-GLP toxicokinetics study conducted according to OECD TG 417 was performed with male rabbits (strain not identified, 4 total) administered cutaneous applications of 10 mg ^{14}C-radiolabled dodecyldimethylamine oxide (greater than 98.5% purity, 1.3 µCi/g) in water to shaved skin. Following a 72-hour continuous cutaneous exposure, 51% of the administered radioactivity was measured in the excrement and body tissues excluding the application site. Total recovery in the blood was 0.03 µg/g and total tissue recovery was 5.1%. Total recovery of the administered radioactivity was 42.1% in the urine, 2.22% in the feces, and 1.4% in the exhaled air.
- A pre-GLP toxicokinetics study conducted according to OECD TG 417 was performed with male mice (strain not identified, 3 total) administered 1 mg ^{14}C-radiolabled dodecyldimethylamine oxide (greater than 98.5% purity, 1.3 µCi/g) in water to shaved skin. Following a 72-hour continuous cutaneous exposure, 36% of the administered radioactivity was measured in the excrement and body tissues excluding the application site. Total recovery in the blood was 1.10 µg/g and total tissue recovery was 17.62%. Total recovery of the administered radioactivity was 11.6% in urine, 1.4% in feces, and 5.0% in exhaled air.
- A non-GLP-compliant toxicokinetics study conducted according to OECD TG 417 was performed with Sprague-Dawley rats (2 males and 3 females) administered single oral doses of ^{14}C-radiolabled dodecyldimethylamine oxide (purity not specified, 10 mCi/g) in water at 1 mg/kg. The maximum radioactivity level in blood was measured 1.5 hours after dosing. Approximately 60% of the radioactivity was eliminated via the urine, with 30% being eliminated as $^{14}C\ CO_2$ in exhaled air. Less than 10% of the radioactivity was measured in the feces. No sex-related differences were identified in the pattern of excretion. A total of 10 metabolites were identified from urine samples, with the primary metabolites being N,N-dimethyl-N-oxide-4-aminobutyric acid and N,N-dimethyl-4-aminobutyric acid.

- In summary, rapid absorption of dodecyldimethylamine oxide is observed following oral doses, with peak blood levels reached 1-1.5 hours after dosing. Dodecyldimethylamine oxide is rapidly excreted into the urine and to a lesser extent via exhaled air. It is excreted to a lesser degree via the feces. Although dermal absorption was limited in human volunteers (<8%), 36-51% of the administered dose was absorbed following 72-hour continuous cutaneous exposures in mice and rabbits. Dodecyldimethylamine oxide is metabolized *in vivo* with N,N-dimethyl-N-oxide-4-aminobutyric acid and N,N-dimethyl-4-aminobutyric acid being the primary metabolites.

Hazard Classification Summary Section:
In order to classify the hazards of dodecyldimethylamine oxide using data from the highest quality studies, only studies with Klimisch scores of 1 (reliable without restriction) or 2 (reliable with restriction) were included in this assessment unless otherwise mentioned. When studies with Klimisch scores of 3 (not reliable) or 4 (not assignable) were identified, ToxServices included a statement indicating that they are available in their respective references.

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L

Dodecyldimethylamine oxide was assigned a score of Low for carcinogenicity based on negative carcinogenicity test results obtained with dodecyldimethylamine oxide when administered in drinking water alone or with the analog amines, C10-16-alkyldimethyl, N-oxides in feed or via dermal application. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data, negative studies, no structural alerts, and no GHS classification are available (CPA 2016b). The confidence in the score is high as it is based on a weight of evidence involving well-documented studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - A 93-week carcinogenicity study (GLP compliance and guideline not reported) with a post-exposure observation period of 34-37 weeks was negative for carcinogenicity. Male and female Fischer 344 rats (number not reported; identified as 24/sex/dose group in HSDB 2009) were provided drinking water containing dodecyldimethylamine oxide (purity not reported) at 10,000 ppm (0.1% or 250 mg/kg) 5/days/week with or without 2,000 ppm (0.2%) sodium nitrite. No treatment-related effects were observed on tumor incidence or type following treatment with dodecyldimethylamine oxide alone. An increased incidence of liver tumors was observed in male animals when treatment was administered as dodecyldimethylamine oxide and sodium nitrite. The authors concluded that treatment with dodecyldimethylamine oxide and sodium nitrite resulted in the formation of at least 1 carcinogenic nitrosamine.
- Analog: Amines, C10-16-alkyldimethyl, N-oxides (CAS #70592-80-2)
  - OECD 2006
    - A GLP-compliant two-year carcinogenicity test was performed with CD-1 mice (75/sex/dose group) administered dermal doses of amines, C10-16-alkyldimethyl, N-oxides (27% purity, majority C12) in water at 0.05%, 0.13% or 0.26% to clipped skin three days per week for 104 weeks. High dose males exhibited a decrease in overall survival, but the values were within the historical variability for controls. No treatment-related effects were observed on mean body weights or organ weights. High dose animals exhibited dermal irritation effects as diffuse acanthosis and hyperkeratosis. No treatment-related skin or systemic neoplasms were observed.
    - A non-GLP-compliant two-year carcinogenicity test was performed with Charles River rats (60/sex/dose group) provided feed containing amines, C10-16-alkyldimethyl, N-oxides (27% purity, majority C12) at 0, 0.01, 0.1, or 0.2%. There were no significant differences in survival at 104 weeks or in mean feed consumption across treatment groups. There was no evidence of a carcinogenic response after chronic dietary administration of amines, C10-16-alkyldimethyl, N-oxides.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L

Dodecyldimethylamine oxide was assigned a score of Low for mutagenicity/genotoxicity based on negative results for mutagenicity obtained *in vitro* and *in vivo* for dodecyldimethylamine oxide and negative results for clastogenicity for the analog N,N-dimethyl-1-methyldodecylamine oxide.

GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data for mutagenicity and clastogenicity, negative studies, no structural alerts, and no GHS classification are available (CPA 2016b). The confidence in the score is high as it is based on a weight of evidence incorporating high quality and/or well documented studies.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
    - *In vitro*: Negative results for mutagenicity were obtained in an Ames test when dodecyldimethylamine oxide is tested alone. *Salmonella typhimurium* tester strains TA1535, TA1538, TA100, and TA98 were exposed to dodecyldimethylamine oxide (purity not specified) at 250 µg/plate with and without metabolic activation. Cytotoxicity was observed in TA1535 at the 250 µg/plate concentration. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation. After nitrosation with nitrous acid, however, the N-nitroso derivative of dodecyldimethylamine oxide was mutagenic with S9 activation in TA1535, and study authors report similar results with S9 from hamsters and rats.
    - *In vitro*: Negative results for genotoxicity were obtained in a cell transformation assay. Syrian hamster embryo cells were exposed to dodecyldimethylamine oxide (29.1% purity) at 0.1-20 µg/mL. On gestational days 13 and 14, pregnant hamsters were killed to procure target and feeder layer cells, respectively. On days 0-5, feeder layer cells were thawed and plated, target cells were thawed and plated, feeder cells were irradiated, and target cells were added to irradiated feeder cells. The exposures were applied on day 6 with 7-9 dishes per dose and fixation and staining occurred on day 14. The study authors identified cytotoxicity at 10-20 µg/mL dodecyldimethylamine oxide but no evidence of transformation was observed.
        - Please note that although the test substance used in this study was identified as dodecyldimethylamine oxide (CAS #1643-20-5), the carbon chain length distribution was identified as 0.8% C10, 97.5% C14 and 1.7% C17. Dodecyldimethylamine oxide has a C12 alkyl chain.
    - *In vitro*: Negative results for mutagenicity were obtained in an Ames test. *S. typhimurium* tester strains TA98 and TA100 were exposed to dodecyldimethylamine oxide (29.1% purity) in DMSO at 10-200 µg/plate with and without metabolic activation. Cytotoxicity was reported at 100-200 µg/plate without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation.
        - Please note that although the test substance used in this study was identified as dodecyldimethylamine oxide (CAS #1643-20-5), the carbon chain length distribution was identified as 0.8% C10, 97.5% C14 and 1.7% C17. Dodecyldimethylamine oxide has a C12 alkyl chain.
- ECHA 2016
    - *In vitro*: Negative results for mutagenicity were obtained in a GLP-compliant Ames test conducted according to OECD TG 471. *S. typhimurium* tester strains TA 100, TA 1535, TA 1537, TA 1538, and TA 98 were exposed to dodecyldimethylamine oxide (as 30% lauryldimethylaminoxide, 70% water) in DMSO at up to 10,000 µg/plate with and without metabolic activation. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.
    - *In vivo*: Negative results for mutagenicity were obtained in a non-GLP-compliant dominant lethal test conducted in a manner similar to OECD TG 478 (no positive control). Male

C3D2F1/J mice (20/dose group) were administered oral doses of dodecyldimethylamine oxide (purity not specified) in water at 10, 100, or 1,000 mg/kg/day for 5 consecutive days. Immediately after the last dose, each male was caged separately with two untreated virgin female C3D2F1/J mice for seven days. The authors indicated that this mating procedure was continued weekly for an additional six weeks, thus encompassing the entire spermatogenic cycle of the mouse. On day 13 or 14 of pregnancy (as measured from the mid-week of presumptive mating), the females were sacrificed and the total number of implantations, resorptions, and dead embryos were identified (OECD 2006 notes that the number or corpora lutea were not counted). No treatment-related effects were observed on these parameters.

- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - *In vitro*: Negative results for mutagenicity were obtained in a GLP-compliant mammalian cell gene mutation assay conducted according to EU Method B.17. Chinese hamster lung fibroblasts (V79) were exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (28-30% w/w) in water at 0.313-5.0 µg/mL without metabolic activation and 0.625-10 µg/mL with metabolic activation. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.
- Analog: N,N-Dimethyl-1-methyldodecylamine oxide (CAS #60729-78-4)
    - ECHA 2016
        - *In vivo*: Negative results for clastogenicity were obtained in a non-GLP-compliant micronucleus assay. Chinese hamsters (5/sex/dose group) were administered a pair of intraperitoneal injections of N,N-dimethyl-1-methyldodecylamine oxide (purity not specified) in water at 0, 160, 300, or 700 mg/kg separated by 24 hours. Six hours after the second dose was administered, the animals were sacrificed and tissues (not specified) were isolated for the assessment of micronuclei. No increase in the frequency of micronuclei was observed with treatment.
        - *In vivo*: Negative results for clastogenicity were obtained in a non-GLP-compliant micronucleus assay. ICR mice (12 animals total) were administered single oral doses of N,N-dimethyl-1-methyldodecylamine oxide (purity not specified) in water at 0 or 235 mg/kg. The animals were sacrificed 6, 24, 48, or 72 hours after treatment and tissues (not specified) were isolated for the assessment of micronuclei. No increase in the frequency of micronuclei was observed with treatment.
        - *In vivo*: Negative results for clastogenicity were obtained in a non-GLP-compliant chromosome aberration assay. Chinese hamsters (5/sex/dose group) were administered intraperitoneal injections of N,N-dimethyl-1-methyldodecylamine oxide (purity not specified) in water at 0, 160, 300, or 700 mg/kg. The number of injections was not specified but it is likely that the same procedure as the study listed above was followed, meaning that a pair of injections was administered 24 hours apart and the animals were sacrificed 6 hours after the second dose was administered. A total of 250 metaphase cells/concentration were analyzed. No increase in the frequency of chromosome aberrations was observed with treatment.

Reproductive Toxicity (R) Score (H, M, or L): *M*
Dodecyldimethylamine oxide was assigned a score of Moderate for reproductive toxicity based on the effects to post-implantation loss and gestation index in a combined repeated dose toxicity study with the

reproduction / developmental toxicity screening test. GreenScreen® criteria classify chemicals as a Moderate hazard for reproductive toxicity when limited or marginal evidence of reproductive toxicity is observed in animals (CPA 2016b). The confidence in the score is low as it is not clear if the observed adverse reproductive effects are secondary to systemic toxicity.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - A non-GLP-compliant two-generation reproductive toxicity study conducted according to the Japanese Ministry of Health and Welfare Guidelines was performed in Charles River CD rats (15 males/group, 30 females/group) provided diets containing dodecyldimethylamine oxide (30.0% purity) at 0, 750, 1,500, or 3,000 ppm for 6.5 weeks and then reduced to 0, 188, 375, and 750 ppm, respectively, for the remainder of the study due to marked reductions in body weight. The equivalent doses were 0, 11, 20, and 40 mg/kg/day, respectively. The animals were treated for 101-120 days prior to mating and then through the mating, gestation, and lactation periods. The F1 animals were provided diets containing dodecyldimethylamine oxide at 0, 188, 375, and 750 ppm for 120 days prior to mating. The animals were evaluated for somatic growth development, fertility, reproductive function, bodyweight gain, weekly food consumption, gross pathology, and histopathology. Slight reductions in weight gain of parents and offspring were observed (did not exceed 10%), but no effects were displayed on mating performance and fertility. For all treated animals, absolute bodyweights of both sexes was slightly below that of controls, though no effects were evident in mating performance, fertility, or conception rate in either generation. There were no effects observed on gestation or parturition. Slightly fewer F2 offspring were born at 750 ppm, but they and the F1 offspring displayed no treatment-related effects on litter size at birth, live birth index, or birthweight. Viability of the F1 offspring was not affected with treatment, but was reduced in F2 offspring at 188 and 750 ppm. However, the values were within range of historical controls and the effects were not dose-dependent. Both the F1 and F2 offspring exhibited non-statistically significant reductions in bodyweight gain during lactation (not greater than 10%) at 1, 4, 11, and 18 days *post-partum*. Reductions in body weight were statistically significant 25 days *post-partum* for the 2 highest doses in F1 and F2 offspring, but this was not considered an adverse effect because this only occurred when rat pups were getting most of their calories from solid food and it was not due to treatment. There were no macroscopic or histopathological effects observed with treatment. No treatment-related effects were observed on mean number of litters, mean number of pups per litter, mean live birth index, or mean viability index for the F1 and F2 generations of offspring. The study authors assigned a parental, F1 offspring, and F2 offspring NOAEL of 40 mg/kg/day based on the lack of adverse effects observed on reproduction in this study.
- ECHA 2016
  - A GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD TG 422 was performed with HanRcc: WIST(SPF) rats (10/sex/dose group) administered oral doses of dodecyldimethylamine oxide (30.27%) in water at 0, 40, 100, or 250 mg/kg/day via gavage. Males were dosed for at least 28 days and females were dosed for 14 days prior to mating, through mating and gestation periods, and until postnatal day 4. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, estrous cyclicity, sperm parameters, reproductive indices, and weights, gross pathology, and histopathology of the reproductive organs. High dose males and females exhibited reduced mean body weights

and mean body weight gains throughout the study, while mid dose males exhibited decreased mean body weights during the pre-mating period. Food consumption for high dose males was reduced throughout the treatment period. Mid and high dose females exhibited decreased mean food consumption in a dose-dependent manner during the pre-mating and gestational periods. High dose females still exhibited decreased food consumption during the lactation period. No treatment-related effects were observed on estrous cyclicity, sperm parameters, mean pre-coital time, fertility index, conception rates, or implantation rate. The gestation index was reduced in the high dose group as two dams did not deliver any pups and one dam delivered only one dead pup. Correspondingly, an increase in post-implantation loss was observed in the high dose group. No histopathological changes were observed in the reproductive organs. The study authors identified a reproductive toxicity NOAEL and LOAEL of 100 and 250 mg/kg/day based on the increased rate of post-implantation loss and decreased gestation index observed in the high dose group.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): *M*
Dodecyldimethylamine oxide was assigned a score of Moderate for developmental toxicity based on treatment-related effects on fetal growth, viability, and ossification occurring in the presence of maternal toxicity. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when limited or marginal evidence of developmental toxicity is observed in animals (CPA 2016b). The confidence in the score is reduced as it is not clear if the observed developmental effects were secondary to maternal toxicity.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - A non-GLP-compliant prenatal developmental toxicity study conducted according to the Japanese Ministry of Health and Welfare Guidelines was performed with pregnant female Charles River CD rats (32/dose group) administered oral doses of dodecyldimethylamine oxide (30.0% purity) at 0, 50, 100, or 200 mg/kg/day via gavage on gestational days 7-17. The two-thirds of the dams were sacrificed on gestational day 20 while the remaining one-third were allowed to give birth and allowed to rear their young until postnatal day 25. The maternal evaluations included body weights, food consumption, and ovarian and uterine content. Fetal examinations included fetal weight, sex, and external, skeletal, and visceral abnormalities. Neonatal examinations included litter size at birth, birth-weight of each offspring, sex ratio, and post-natal development, which includes physical development, auditory and visual function, activity, behavior, learning, and locomotor function. A selection of F1 offspring (22/sex) were paired when 10 weeks old, and the females were weighed weekly until mating, and then 0, 2, 7, 9, 11, 13, 15, 17, and 20 days after mating during gestation. On the 20th day after mating, females were killed and uterine contents were examined as described above. Slight decreases in maternal bodyweight gain and food intake (both < 10%) and increase in water intake were observed at the highest dose level. Also at the highest dose level, reduced mean fetal weight due to slowed fetal ossification was observed in females killed on gestational day 20. F1 offspring did not display any effects on litter, parturition, survival, growth, or development. All subsequent growth, mating performance, and fertility of the F1 offspring were similar in control and treatment groups. F1 females from F0 females administered the highest dose, however, displayed slightly higher fetal and placental weights compared to controls, and no effects were seen at

the dose level of 50 or 100 mg/kg/day on the pregnancy or outcome of pregnancy. In addition, no treatment-related effects were observed at the macroscopic level at the necropsy of F1 offspring. The study authors assigned a maternal and teratogenicity NOAEL and LOAEL of 100 and 200 mg/kg/day, respectively, based on changes to maternal and fetal body weights.

- A non-GLP compliant prenatal developmental toxicity test conducted according to the Japanese Ministry of Health and Welfare Guidelines was performed with pregnant female New Zealand white rabbits (14/dose group) administered oral doses of dodecyldimethylamine oxide (30.0% purity) at 0, 40, 80, or 160 mg/kg/day via gavage on gestational days 6-18. The animals were sacrificed on gestational day 29. Maternal evaluations included body weights, food consumption, and ovarian and uterine content. Fetal evaluations included external and skeletal malformations. No effects were observed on *in utero* survival or development with treatment. Maternal bodyweight gain was decreased in the mid and high dose groups. Three females from each of the 80 and 160 mg/kg/day died or were killed *in extremis*, but this observation did not seem to be a result of the treatment. Though bodyweight gain and food and water intake was lower for all treatment groups, they were all less than 10%. No treatment-related effects were observed on litter, development, or teratogenic responses. The study authors assigned a maternal and teratogenicity NOAEL of 160 mg/kg/day based on the lack of treatment-related effects observed on development in this study.

- ECHA 2016
  - A GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD TG 422 was performed with HanRcc: WIST(SPF) rats (10/sex/dose group) administered oral doses of dodecyldimethylamine oxide (30.27%) in water at 0, 40, 100, or 250 mg/kg/day via gavage. Females were dosed for 14 days prior to mating, through mating and gestation periods, and until postnatal day 4. The maternal evaluations included clinical signs of toxicity, body weight, and food consumption, and the offspring evaluations consisted of viability, clinical signs of toxicity, body weight, sex ratio, organ weights, gross pathology, and histopathology. High dose females exhibited reduced mean body weights and mean body weight gains throughout the study. Mid and high dose females exhibited decreased mean food consumption in a dose-dependent manner during the pre-mating and gestational periods. High dose females still exhibited decreased food consumption during the lactation period. In the high dose group, a significant increase in pup death was observed on postnatal days 0-4. Mean pup weight development was depressed in the high dose group during the postnatal period. No treatment-related effects were observed on the pup sex ratio, gross pathological observations, or histopathological findings. The study authors identified a developmental toxicity NOAEL and LOAEL of 100 and 250 mg/kg/day, respectively, based on decreased pup viability and growth observed in the high dose group.

- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
  - ECHA 2016
    - A GLP-compliant prenatal developmental toxicity test conducted according to EPA OTS 798.4900 was performed with pregnant female Sprague-Dawley rats (25/dose group) administered oral doses of amines, C12-14 (even numbered) -alkyldimethyl, N-oxides (purity not specified) in sterile water at 0, 25, 100, or 200 mg/kg/day via gavage on gestational days 6-19. Maternal examinations consisted of clinical signs of toxicity, body weight, food consumption, and ovarian and uterine content. Fetal

examinations consisted of evaluating the incidence of external, visceral, skeletal, and head malformations. Two dams died in the high dose group, with one being attributed to the treatment and the other being an intubation error. Clinical signs of toxicity in the dams in the mid and high dose groups included excessive salivation, rales, urine-stained abdominal fur, brown or red perioral substance, labored breathing, and gasping. Dams in the mid and high dose groups exhibited significantly reduced body weight gains, while high dose dams also exhibited decreased body weights and gravid uterine weights. In the high dose group fetal body weights and live litter size were significantly reduced. The number of early resorptions was increased in the high dose group but was attributed to one dam that had 16 early resorptions. The percentages of fetuses and litters with alterations in the high dose group were significantly increased and involved delays in skeletal ossification, including an increased incidence of bifid thoracic vertebrae centra, incompletely and/or not ossified 1st or 2nd sternal centra, incompletely ossified pubes and significant decreases in the numbers of ossified caudal vertebrae, sternal centers and metacarpals. Delays in ossification also occurred in the mid dose group as an increase in the litter incidence of bifid thoracic vertebrae centra was observed. The study authors identified a maternal NOAEL and LOAEL of 25 and 100 mg/kg/day, respectively, based on changes to maternal body weights, and a developmental toxicity NOAEL and LOAEL of 25 and 100 mg/kg/day, respectively, based on delays in ossification.

Endocrine Activity (E) Score (H, M, or L): DG
Dodecyldimethylamine oxide was assigned a score of Data Gap for endocrine activity based on a lack of data identified for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- No data were identified for this endpoint.

Group II and II* Human Health Effects (Group II and II* Human)
Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): M
Dodecyldimethylamine oxide was assigned a score of Moderate for acute toxicity based on an oral LD_{50} of 1,064 gm/kg in Sprague-Dawley rats. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when oral LD_{50} values are greater than 300 to 2,000 mg/kg (CPA 2016b). Confidence in this score is high as it is based on data from a high quality study.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.

- ECHA 2016
  - *Oral:* LD_{50} (Sprague-Dawley rat) = 1,064 mg/kg (pre-GLP, OECD TG 401)
  - *Dermal:* LD_{50} (New Zealand White rabbit) = greater than 560 mg/kg (pre-GLP, similar to OECD TG 402)
- OECD 2006
  - *Inhalational:* 4-hour aerosol LC_{50} (Sprague-Dawley albino rat) = greater than 0.016 mg/L (GLP-compliant)
  - Acute oral toxicity tests were identified in the SIDS document. However, they were assigned Klimisch scores of 3 (not reliable) or 4 (not assignable). Therefore, ToxServices did not include them in this assessment.
- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
  - ECHA 2016
    - *Oral*: LD_{50} (Wistar rat) = greater than 600 mg/kg (GLP-compliant, OECD TG 401)
    - *Oral:* LD_{50} (Sprague-Dawley rat) = greater than 600 mg/kg (GLP-compliant, OECD TG 401)
    - *Oral:* LD_{50} (rat) = greater than 600 mg/kg (pre-GLP)
    - *Oral:* LD_{50} (Sprague-Dawley rat) = greater than 300 mg/kg (pre-GLP)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)* (vH, H, M, or L):** *H*
Dodecyldimethylamine oxide was assigned a score of High for systemic toxicity (single dose) based on lung pathology in an acute oral toxicity study with an oral LOAEL of 588 mg/kg. GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (single dose) when oral LOAELs are between 300 and 2,000 mg/kg (CPA 2016b). The confidence in the score is reduced as the effects in the lung were found only in one of the 5 oral studies performed with the target compound and surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - *Inhalation:* In the acute inhalation toxicity test that identified a 4-hour aerosol LC_{50} greater than 0.016 mg/L in Sprague-Dawley albino rats, no treatment-related effects were observed on mortality, clinical signs of toxicity, body weights, or gross pathological findings.
- ECHA 2016
  - *Oral:* In the acute oral toxicity study that identified an oral LD_{50} of 1,064 mg/kg in Sprague-Dawley rats, clinical signs of toxicity included decreased motor activity and salivation, and diarrhea was observed in all but the 2,100 mg/kg group (doses tested were 1,500-5,800 mg/kg of 28% w/w dodecyldimethylamine oxide). Piloerection was observed at 4,100 and 5,800 mg/kg, and blanching and nasal hemorrhaging were observed at 2,100-5,800 mg/kg. Slight losses in body weight were observed in the 5,800 mg/kg group (i.e. 1,628 mg active ingredient (a.i.)/kg). No gross pathological changes were observed at 1,500 mg/kg. Gross pathological changes observed at higher dose levels included tan discoloration and pale lungs at 2,100 mg/kg (588 mg/kg a.i.) and greater, gas and/or fluid in the stomach and intestines at 2,100 mg/kg and greater, petechiae (small red or purple spot caused by bleeding into the skin) on the lungs at 3,000 (840 mg/kg a.i.) and 5,800 mg/kg, and liver-colored lungs at 5,800 mg/kg.
    - Lung pathology was also found in a subchronic toxicity study on an analog as described below. This may be related to aspiration of the compound, but the

possibility of target organ toxicity cannot be ruled out. ToxServices identified a LOAEL at 588 mg/kg a.i. based on tan discoloration and pale lungs.

- *Dermal:* In the acute dermal toxicity study that identified a dermal LD_{50} greater than 560 mg/kg in New Zealand White rabbits, males appeared normal during the observation period but 1/3 females exhibited hypoactivity, decreased limb tone, ataxia, and anorexia. No treatment-related effects on body weight or gross pathological findings were observed.

- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
  - ECHA 2016
    - *Oral*: In the acute oral toxicity study that identified an oral LD_{50} greater than 600 mg/kg in Wistar rats, no clinical signs of toxicity, changes to body weight, or gross pathological changes were observed with treatment.
    - *Oral:* In the acute oral toxicity study that identified an oral LD_{50} greater than 600 mg/kg in Sprague-Dawley rats, clinical signs of toxicity included piloerection and hunched posture 1-4 hours after dosing. The animals appeared normal 24 hours after dosing and for the remainder of the observation period. No treatment-related effects were observed on body weights. Gross pathological changes included scattered white raised areas covering approximately 25% of the non-glandular region of the stomach.
    - *Oral:* In the pre-GLP acute oral toxicity study that identified an oral LD_{50} greater than 600 mg/kg in rats, no deaths and no overt signs of toxicity were observed with treatment.
    - *Oral*: In the pre-GLP acute oral toxicity study that identified an oral LD_{50} greater than 300 mg/kg in Sprague-Dawley rats, there were no deaths or overt signs of toxicity evident during the 14-day observation period at up to 5 g/kg of a 6% w/w aqueous solution of amines, C12-14 (even numbered)-alkyldimethyl, N-oxides. At 15.1 g/kg of a 6% w/w aqueous solution of amines, C12-14 (even numbered)-alkyldimethyl, N-oxides, all ten rats were lethargic within 4 hours of dosing and two animals per sex died 24 hours after dosing and an additional 2 males and 1 female died 48 hours after dosing. The remaining three rats survived until the scheduled sacrifice and showed no overt signs of toxicity from Day 3 onwards.

Group II* Score (repeated dose) **(H, M, or L):** *M*

Dodecyldimethylamine oxide was assigned a score of Moderate for systemic toxicity (repeated dose) based on ToxServices classifying it as a GHS Category 2 repeated dose systemic toxicant via the oral route. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when they are classified as GHS Category 2 oral repeated dose systemic toxicants (CPA 2016b). Confidence in this score is low based on the ranges of NOAEL and LOAEL values that straddle the GHS guidance values, precluding their use to support or reverse the classification of dodecyldimethylamine oxide under GHS criteria.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - *Dermal*: A GLP-compliant 4-week repeated dose toxicity test was performed with New Zealand white rabbits (5/sex/dose) administered topical applications of dodecyldimethylamine oxide (0.3%; remainder is 85-95% water, 1-5% PVP/VA copolymer, 0-2% cocamide DEA, 0-2% polyquaternium-11, and < 1% other minor ingredients) at 2

mL/kg/day (equivalent to 6 mg/kg/day) 5 times per week. The animals were evaluated for clinical signs of toxicity, dermal irritation, body weights, organ weights, and histopathology. All animals survived to week 5 and no effects were seen on the mean body weight, clinical observations, mean absolute organ weight, and organ-to-body weight ratios between control and treatment, though slight-moderate erythema was observed in treated females, and slight edema, atonia, fissuring, and slight-moderate desquamation were displayed in treated animals of both sexes. A high incidence of sub-acute inflammation was observed in control and treatment groups at the site of application. There were no other treatment-related effects reported. The study authors concluded this formulation at 2 mL/kg/day (6 mg/kg/day) is slightly irritating and assigned a NOEL of 6 mg/kg/day for systemic effects.

- ECHA 2016
    - *Oral:* A GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD TG 422 was performed with HanRcc: WIST(SPF) rats (10/sex/dose group) administered oral doses of dodecyldimethylamine oxide (30.27%) in water at 0, 40, 100, or 250 mg/kg/day via gavage. Males were dosed for at least 28 days and females were dosed for 14 days prior to mating, through mating and gestation periods, and until postnatal day 4, for a total of 40-45 days of exposure. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, functional observational battery, organ weights, gross pathology, and histopathology. No treatment-related effects were observed on hematology, clinical chemistry, or histopathology. Mid and high dose males exhibited decreased activity, and high dose males occasionally exhibited rales and salivation. During the gestation period, rales and salivation were observed in 3 high dose females during the gestational period. Total locomotor activity was reduced in high dose females. High dose males and females exhibited reduced mean body weights and mean body weight gains throughout the study, while mid dose males exhibited decreased mean body weights during the pre-mating period. Food consumption for high dose males was reduced throughout the treatment period. Mid and high dose females exhibited decreased mean food consumption in a dose-dependent manner during the pre-mating and gestational periods. High dose females still exhibited decreased food consumption during the lactation period. High dose males and females exhibited increased absolute and relative liver weights. The mucosa of the forestomach was thickened and had an irregular surface and the stomach was thickened in 5/10 high dose males. Histopathological evaluations identified lymphoid depletion of the spleen in 2/5 high dose females, hepatocellular hypertrophy in 2/5 males and 1/5 females in the high dose group, and increased severity of tabular basophilia and hyaline droplets in the kidneys of high dose males. Hyperkeratosis, parakeratosis, squamous cell hyperplasia and submucosal inflammation of the forestomach in all mid and high dose males and females. Submucosal edema was observed in 3/5 males and 3/5 females in the high dose group and in mid dose females (number not specified). Erosion of the forestomach was observed in 3/5 high dose males and 3/5 high dose females, while ulcerations of the forestomach were observed in 1/5 female in each of the mid and high dose groups. Pustules of the forestomach were observed in 2/5 high dose males and in 1/5 females in the mid and high dose groups. The study authors identified a NOAEL and LOAEL of 40 and 100 mg/kg/day, respectively, based on histopathological changes observed in the mid and high dose groups.
        - As the duration of this study was less than 90 days, ToxServices modified the GHS guidance values of 10 and 100 mg/kg/day for a repeated oral dose study (UN 2015) by a factor of 3 for males (28 days is approximately one-third of 90 days) and 2 for females (40-45 days is approximately one-half of 90 days) to 30 and 300 mg/kg/day

and 20 and 200 mg/kg/day, respectively. Since the LOAEL of 100 mg/kg/day is less than 300 and 200 mg/kg/day, ToxServices classified dodecyldimethylamine oxide as a GHS Category 2 oral repeated dose toxicant.

- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - *Oral:* A non-GLP-compliant subchronic repeated dose toxicity study conducted according to OECD TG 408 was performed with Sprague-Dawley rats (20/sex/dose group) provided diets containing amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (purity not specified) at 0%, 0.1%, 0.2%, or 0.4% (equivalent to 0, 88, 176, or 353 mg/kg/day, respectively) for 13 weeks. The animals were evaluated for clinical signs of toxicity, body weight, body weight gain, food consumption, hematology, clinical chemistry, urinalysis, organ weights, gross pathology, and histopathology. No treatment-related effects were observed on clinical signs of toxicity, urinalysis parameters, gross pathological observations, or histopathological observations. Statistically significant decreases in mean body weights were observed for high dose males and females during weeks 1-13 and for mid dose females from weeks 3-5 and 9-13. Decreased food consumption was observed in the mid and high dose females and males in all treatment groups periodically during the treatment period. In the high dose group, lenticular opacities pertaining to the posterior cortex of the lens were observed in high dose males and females at 6 and 13 weeks. Statistically significant changes to hematology parameters at week 7 included increased mean erythrocyte counts observed in males of all three treatment groups and in mid dose females, and decreased mean leukocytes counts observed in high dose males and in low and high dose females. Statistically significant changes to clinical chemistry parameters at week 7 included decreased mean glutamic pyruvic transaminase levels observed in high dose males, decreased mean serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase levels in mid and high dose group females, decreased mean blood urea nitrogen levels in mid dose females, increased mean fasting glucose levels in mid dose females, decreased serum glutamic oxaloacetic transaminase in mid dose males and high dose females, and decreased serum glutamic pyruvic transaminase in high dose males and females in all three treatment groups. At week 13, increased mean alkaline phosphates levels were observed in high dose females and increased blood urea nitrogen levels were observed in high dose male and mid dose females. Changes to organ weights included decreased mean terminal body weights in high dose males, increased mean relative testes and brain weights in the mid and high dose males, and increased relative kidney weights in the low and high dose males. Mid and high dose females exhibited increased mean relative heart weights. The study authors identified a NOAEL and LOAEL of 88 and 176 mg/kg/day, respectively, based on changes to body weights.
            - ToxServices noted that the reduced body weight may be related to reduced food intake and reduced feed efficiency, which the study authors attributed to stress caused by ophthalmology examination and blood collection. The increased relative organ weight may also be an artifact of reduced body weight. The extent of changes in body weight, organ weights and other parameters was not reported, and therefore it is impossible to determine the biological significance of the reported findings.

- *Oral:* A non-GLP-compliant repeated dose toxicity study conducted in a manner similar to OECD TG 408 (rabbits used rather than rat or mouse, treatment for the low and mid dose groups was extended past 13 weeks) was performed with New Zealand White rabbits (25/sex/dose group) provided diets containing amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (purity not specified) at 0.1, 0.5, or 1.0% for 13 weeks. The study authors identified a food consumption factor of 0.032 kg diet/kg bodyweight/day; therefore, the equivalent doses were 32, 160, and 320 mg/kg/day, respectively. After 13 weeks, high dose animals were sacrificed but low and mid-dose animals and control animals were treated for an additional 19 weeks and sacrificed at 32 or 33 weeks. The animals were evaluated for clinical signs of toxicity, body weights, food consumption, hematology, clinical chemistry, organ weights, gross pathology, and histopathology. During the first week of treatment, anorexia was observed in 1 mid dose animal and 5 high dose animals (sex not specified). Anorexia was also observed sporadically in all groups during the remainder of the treatment period but with a higher incidence in the high dose group relative to the other groups. Additional clinical signs of toxicity were listlessness, hyperpnea, alopecia, wheezing, thinness, and rough fur coat. Statistically significantly decreased terminal body weights were observed in high dose males, and decreased food consumption was observed in high dose males and females. Changes to hematology values at week 13 included significantly decreased mean hematocrit and hemoglobin values in high-dose males and females and decreased erythrocyte and mean corpuscular hemoglobin values in high-dose females. Treatment-related changes to clinical chemistry parameters at week 13 included increases in total bilirubin values in high dose males and mid and high dose females and decreased mean alkaline phosphatase values in high dose males and females. Mid dose males exhibited decreased mean alkaline phosphatase values at week 32. Mid dose males exhibited increased relative liver body weights at sacrifice. High dose males and females exhibited enlarged cervical and mesenteric lymph nodes, purulent material (including abscesses) in the lungs, and an absence of body fat. Histomorphologic alterations in the lung, spleen, small intestine, and mesenteric lymph node characterized by the presence of large foamy appearing macrophages and marked vacuolation of the bronchial epithelium present in the lung sections were observed in high dose animals in these tissues. The study authors identified a NOAEL of 0.1% (equivalent to 32 mg/kg/day) and LOAEL of 0.5% (equivalent to 160 mg/kg/day) based on changes to body weights, gross pathological findings, and histopathological findings.
- *Oral:* A non-GLP-compliant repeated dose toxicity study conducted in a manner similar to OECD TG 408 (included interim sacrifice) was performed with Sprague-Dawley rats (20/sex/dose group) provided diets containing amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (purity not specified) at 0, 0.02, 0.1, or 0.5% (equivalent to 0, 17.6, 88, and 440 mg/kg/day, respectively) for 13-14 weeks. An interim sacrifice incorporating 5 animals per sex per dose group was performed at week 4. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. No treatment-related effects were observed for hematology, clinical chemistry, or urinalysis. A slightly higher frequency of incidental clinical signs of toxicity, including rough fur coat, hunched posture, stains on fur coat, and soft feces, was observed in the high dose group. Significantly reduced body weight gain and food consumption were observed in the high dose group. The study authors

indicated that the high dose animals were reluctant to consume the diet due to palatability of the feed. The high dose group animals exhibited a number of statistically significant changes to absolute and relative organ weights. However, the terminal body weight values were significantly lower than the concurrent controls. The study authors, therefore, concluded that the changes to organ weights were likely a reflection of the growth retardation observed for this dose group. High dose animals exhibited a dark liver color due to a decreased fatty tissue content. No histopathological changes were observed in internal tissues with treatment. Two high dose males and two high dose females exhibited bilateral lenticular cataracts. The study authors identified a NOAEL and LOAEL of 88 and 440 mg/kg/day based on decreased body weights and bilateral cataracts.

  - Additional repeated dose studies were identified in the REACH dossier amines, C12-14 (even numbered)-alkyldimethyl, N-oxides. However, they tested only one dose level or were not performed according to an authoritative guideline. Therefore, ToxServices did not include them in this assessment.

- In summary, the results of the combined repeated dose toxicity study with the reproduction / developmental toxicity screening test indicate that dodecyldimethylamine oxide should be classified as a GHS Category 2 oral repeated dose systemic toxicant. The majority of subchronic repeated dose studies have ranges of NOAEL and LOAEL values that include the GHS guidance value of 100 mg/kg/day for oral subchronic repeated dose studies (UN 2015). Therefore, it is not possible to determine if the results of these studies support the classification of dodecyldimethylamine oxide as a repeated dose toxicant under GHS criteria (i.e., adverse effects at 100 mg/kg/day or lower for a 90-day study). Therefore, ToxServices classified dodecyldimethylamine oxide as a GHS Category 2 repeated dose systemic toxicant via the oral route in order to be protective of human health, but assigned a low confidence level to reflect the uncertainty regarding the results of the subchronic studies.

Neurotoxicity (N)

Group II Score (single dose)* (vH, H, M, or L): *vH

Dodecyldimethylamine oxide was assigned a score of Very High for neurotoxicity (single dose) based on ToxServices classifying it as a GHS Category 2 dermal single dose systemic toxicant based on neurotoxicity. GreenScreen® criteria classify chemicals as a Very High hazard for neurotoxicity (single dose) when they are classified as GHS Category 2 dermal single dose systemic toxicants based on neurotoxicity (CPA 2016b). The confidence in the score is low as the effects were only observed in one of three female animals.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- ECHA 2016
  - *Oral:* In the acute oral toxicity study that identified an oral LD_{50} of 1,064 mg/kg in Sprague-Dawley rats, clinical signs of toxicity included decreased motor activity in all but the 2,100 mg/kg group (doses tested were 1,500-5,800 mg/kg of 28% w/w dodecyldimethylamine oxide). The lowest dose, 1,500 mg/kg, is equivalent to 420 mg/kg a.i..
  - *Dermal:* In the acute dermal toxicity study that identified a dermal LD_{50} greater than 560 mg/kg in New Zealand White rabbits, males appeared normal during the observation period but 1/3 females exhibited hypoactivity, decreased limb tone, and ataxia after dermal dosing with 560 mg/kg dodecyldimethylamine oxide.

- Based on the neurotoxicity observed in rabbits following a dermal dose of 560 mg/kg, ToxServices classified dodecyldimethylamine oxide as a GHS Category 2 single dose systemic toxicity based on neurotoxicity (UN 2015). GHS criteria define GHS Category 2 single dose systemic toxicants as chemicals that produce adverse effects at dermal doses no greater than 1,000 mg/kg.

Group II* Score (repeated dose) **(H, M, or L):** *M*

Dodecyldimethylamine oxide was assigned a score of Moderate for neurotoxicity (repeated dose) based on reduced locomotor activity observed in a combined oral reproduction/developmental toxicity study, classifying to GHS Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity when they are classified to GHS Category 2 (CPA 2016b). The confidence in the score is adjusted as the NOAEL and LOAEL straddle the applicable GHS Guidance value, making it impossible to determine if adverse effects could occur at or below the Guidance dose.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- ECHA 2016
    - *Oral:* A GLP-compliant combined repeated dose toxicity study with the reproduction / developmental toxicity screening test conducted according to OECD TG 422 was performed with HanRcc: WIST(SPF) rats (10/sex/dose group) administered oral doses of dodecyldimethylamine oxide (30.27%) in water at 0, 40, 100, or 250 mg/kg/day via gavage. Males were dosed for at least 28 days and females were dosed for 14 days prior to mating, through mating and gestation periods, and until postnatal day 4. The animals were evaluated in a functional observational battery (FOB), males shortly before sacrifice and females on postnatal day 3 or 4. The FOB included cage-side, hand-held, open field, and categorical observations, hind limb/fore limb grip strength, landing foot splay, rectal temperature, and locomotor activity. Total locomotor activity was reduced in high dose females. ToxServices identified a neurotoxicity NOAEL and LOAEL of 100 and 250 mg/kg/day, respectively, based on reduced locomotor activity observed in the high dose group.
        - As the duration of this study was less than 90 days, ToxServices modified the GHS guidance values of 10 and 100 mg/kg/day for a repeated oral dose study (UN 2015) by a factor of 2 for females (40-45 days is approximately one-half of 90 days) to 20 and 200 mg/kg/day, respectively. Since the range between the NOAEL of 100 mg/kg/day and LOAEL of 250 mg/kg/day crosses the adjusted guidance value, it is not possible to determine with confidence if adverse effects could occur at or below the guidance value. ToxServices conservatively classified dodecyldimethylamine oxide to GHS Category 2 in order to be protective of public health..

Skin Sensitization (SnS) Group II* Score (H, M, or L): L

Dodecyldimethylamine oxide was assigned a score of Low for skin sensitization based on negative results for skin sensitization obtained for it and the analog amines, C12-14 (even numbered)-alkyldimethyl, N-oxides. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data, negative studies, no structural alerts, and no GHS classification are available (CPA 2016b). The confidence in the score is high as it is based on a weight of evidence incorporating high quality and/or well-documented studies.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.

- OECD 2006
    - In a GLP-compliant Human Repeat Insult patch Test, a hair styling mousse containing 0.3% dodecyldimethylamine oxide (other ingredients not identified) and diluted at 50% in distilled water applied under occlusive dressing in 101 volunteers was negative for sensitization. The occlusive patch contained a concentration of 0.15% in distilled water. Patches were applied every Monday, Wednesday, and Friday for 3 consecutive weeks on the lateral surface of the upper arm and removed 24 hours later. Patch sites were observed before the next patch application. Challenge patches were applied 17 days after the last induction application and kept on for 24 hours on the original and opposite arm of each volunteer. A maximum score of 1 for mild erythematous reaction (faint pink to definite pink) was assigned by the study authors. The study authors concluded that there was no evidence of sensitization in this study.
    - Additional dermal sensitization studies were identified in the SIDS dossier. However, they were assigned Klimisch scores of 4 (not assignable). Therefore, ToxServices did not include them in this assessment.
- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - A pre-GLP Buehler test conducted according to OECD TG 406 was performed with Hartley guinea pigs (20 treated animals and 10 controls) administered dermal doses of amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (27.8% dodecyl dimethyl amine oxide). The induction doses were applied as 0.4 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides under occlusive dressing for 6 hours once weekly for 3 weeks. Two weeks after the third induction dose, the animals were challenged with a 10% v/v solutions of amines, C12-14 (even numbered)-alkyldimethyl, N-oxides in water under occlusive dressing for 6 hours. Dermal reactions were evaluated at 24 and 48 hours after the challenge dose. At the 24-hour reading, 2/20 (10%) animals exhibited positive dermal reactions, whereas 0/20 animals exhibited positive reactions at the 48-hour reading. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not sensitizing to the skin in this study.
        - A GLP-compliant Buehler test conducted according to OECD TG 406 was performed with Hartley guinea pigs (20 treated animals and 10 controls) administered dermal doses of amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (pure active substance). The induction doses were applied as 0.4 mL 2% w/v amines, C12-14 (even numbered)-alkyldimethyl, N-oxides in water under occlusive dressing for 6 hours weekly for 3 weeks. The challenge dose was applied two weeks after the third induction dose as a 1% w/v aqueous solution under occlusive dressing for 6 hours. The dermal reactions were evaluated 24 and 48 hours after the challenge dose. No positive reactions were observed at these time points and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not sensitizing to the skin in this study.
- Based on the weight of evidence, a score of Low was assigned. All the animal and human studies identified above were negative for skin sensitization.

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG
Dodecyldimethylamine oxide was assigned a score of Data Gap for respiratory sensitization based on a lack of data for this endpoint.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- No data were identified for this endpoint.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): *vH*
Dodecyldimethylamine oxide was assigned a score of Very High for skin irritation/corrosivity based on ToxServices classifying it as a GHS Category 1 dermal irritant. GreenScreen® criteria classify chemicals as a Very High hazard for skin irritation/corrosivity when they are classified as GHS Category 1 dermal irritants (CPA 2016b). The confidence in the score is low as only one study identified necrotic effects to the skin and the observation periods for most studies were too short to demonstrate the reversibility of the dermal irritation effects.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:*
        - New Zealand – GHS – 8.2B: Corrosive to dermal tissue
            - Based on EU R-phrase R34 (Causes burns) listed on an MSDS.
        - Japan GHS - Skin corrosion / irritation - Category 2
            - Based on severe dermal irritation observed in rabbits exposed for 24 hours.
- HSDB 2009
    - A dermal irritation test was performed with 0.5 mL of three formulations containing 30% dodecyldimethylamine oxide was applied to 3 male and 3 female New Zealand white rabbits within separate sites on their clipped backs. The sites received dermal irritation scores of 7.0, 7.2, and 7.6 out of 8 for erythema, eschar, and edema at removal and 48 hours later. Moderate to severe erythema and edema, two cases of necrosis, and one case of necrosis with bleeding fissures were displayed 24 hours later. Severe erythema and edema, eschar, bleeding fissures, necrosis, and thickened skin were observed 72 hours later. GLP compliance, guideline, and Klimisch score were not reported for this study.
- OECD 2006
    - A GLP-compliant study was conducted according to the Human Cumulative irritation 3-Patch Application Test. Ten volunteers were administered topical applications of dodecyldimethylamine oxide (0.45% active) at 0.3%, 0.6%, 0.9%, 1.2%, or 1.5%. Controls were administered water. After 7 days of exposure with the exception of the control and 0.3% concentration, which both resulted in no cumulative irritation, all other concentrations resulted in very mild cumulative irritation. The study authors concluded a 0.45% concentration as appropriate for a planned human repeat insult patch test.
    - A GLP-compliant study (no guideline reported) was performed with 6 New Zealand white rabbits (sex not reported) in which 0.5 mL of a test substance mixture containing 30% dodecyldimethylamine oxide, 30% betaine, and 40% water were administered to shaved (not abraded), dorsal skin sites with occlusive covering for 24 hours. Observations were made at 24 and 72 hours. Moderate irritation was observed at 24 hours, and severe irritation was observed at 72 hours. Erythema scores were moderate to severe and severe at 24 hours and 72 hours, respectively, and edema scores were moderate to severe and severe at 24 hours, and 72 hours, respectively. The mean primary dermal irritation index (PDII) was 7.3.
    - A non-GLP-compliant study was conducted according to HSLA 16, 1500.41 with rabbits (number, sex, and strain not reported) administered 0.5 mL dodecyldimethylamine oxide (5% aqueous solution) to the skin, and observations were made at 24 and 72 hours (study reports information was not given on exposure duration, clipping of fur, abraded skin, or

porous gauze dressing to hold test substance against skin). The results included edema scores of 0-2, erythema scores of 1-2, and a PDII of 2.58 (time of observation for scores not reported).
    - A non-GLP-compliant study was conducted following guideline CFR 21, part 191.1 (g), 191.11 and performed with 6 albino rabbits (sex and strain not reported) in which 0.5 mL undiluted dodecyldimethylamine oxide (5% active) were exposed to the animals for 24 hours on intact, abraded skin. Observations were recorded at 24 and 48 hours, both reporting no display of irritation with a PDII of 0.
    - A study (GLP compliance not reported) presumably conducted according to guideline CFR 21, part 191.1 (g), 191.11 was performed with 6 albino rabbits (sex and strain not reported) administered 0.5 mL undiluted dodecyldimethylamine oxide (5% active) to intact, abraded skin and covered with occlusive dressing for an exposure duration of 24 hours. Both observations at 24 and 48 hours reported no signs of irritation and a PDII of 1.41 was reported.
    - Two additional dermal irritation studies were identified in the SIDS document. However, they were assigned Klimisch scores of 4 (not assignable). Therefore, ToxServices did not include them in this assessment.
- ECHA 2016
    - A pre-GLP dermal irritation test conducted in a manner similar to OECD TG 404 (24-hour exposure rather than a 4-hour exposure) was performed with New Zealand White rabbits (3 females) administered topical applications of 0.4 mL undiluted dodecyldimethylamine oxide (containing 27.8% a.i.) to intact and abraded skin under occlusive dressing for 24 hours. An observation period of 72 hours followed the exposure period. The mean PDII for intact and abraded skin was 1.67/8 at 24 hours and 4/8 at 72 hours. No edema was observed, but erythema scores were 1-2 (max 4) at 24 hours and 4/4 at 72 hours for intact and abraded skin. The erythema was not reversible by the end of the observation period. Slight eschar formation was also observed at 72 hours. The study authors concluded that the test compound was irritating to the skin in this study and classified it as a GHS Category 2 dermal irritant.[12]
- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - A pre-GLP dermal irritation test conducted according to U.S. Federal Register Vol. 41 (188): 24572 (27th September 1976) and U.S. CFR 49 (173) was performed with New Zealand White rabbits (6 total) administered topical applications of 0.5 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (30% w/w) to clipped skin under occlusive dressing for 4 hours. An observation period of 48 hours followed the exposure period. At 48 hours, the mean erythema score was 1.83/4 and the mean edema score was 0/4. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not corrosive to the skin in this study.
        - A pre-GLP dermal irritation test conducted according to U.S. Federal Register Vol. 41 (188): 42572 (27th September 1976) and U.S. CFR 49 (173) was performed with New Zealand White rabbits (6 total) administered topical applications of 0.5 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (30% w/w) to clipped skin under occlusive dressing for 4 hours. An observation period of 48

[12] It is not entirely clear if this study was conducted on the target chemical. The ECHA record provided conflicting information on the tested material.

hours followed the exposure period. At 48 hours, the mean erythema score was 2/4 and the mean edema score was 0.66/4. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not corrosive to the skin in this study.

- A pre-GLP dermal irritation test conducted according to U.S. Federal Register Vol. 38 (187): 1500:41, 1973 was performed with New Zealand White rabbits (6 total) administered topical applications of 0.5 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (6.5%) to intact or abraded skin under occlusive dressing for 24 hours. An observation period of 72 hours followed the exposure period. A primary irritation score of 2.07 was observed over 72 hours. For the animals with intact skin, 4/6 animals exhibited erythema that was not fully reversible by the end of the observation period and 1/6 animals exhibited edema that was not fully reversible by the end of the observation period. At 24 and 72 hours, mean erythema scores ranged from 0.5-1.5 (max 4) and mean edema scores ranged from 0.5-1 (max 4). The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not irritating to the skin in this study.
- A pre-GLP dermal irritation test conducted according to U.S. Federal Register, Vol. 41 (188): 42572 (27th September 1976) and U.S. CFR 49(173) was performed with New Zealand White rabbits (6 total) administered topical applications of 0.5 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (30%w/w) to clipped skin under occlusive dressing for 4 hours. An observation period of 48 hours followed the exposure period. At 48 hours, the mean erythema score was 2.33/4 and the mean edema score was 0.66/4. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not corrosive to the skin in this study.
- A pre-GLP dermal irritation test was performed with New Zealand White rabbits (8 total) administered topical applications of 0.5 mL 0.6% amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (30% purity) in water to abraded and intact skin under occlusive dressing for 24 hours. An observation period of 72 hours followed the exposure period. At 24 and 72 hours, the mean erythema score was 0.5/4 (maximum individual score of 1 at 72 hours and the mean edema score was 0.125/4 (maximum individual score of 1 at 24 hours). The primary irritation index was 0.93. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not irritating to the skin in this study.
- A non-GLP-compliant dermal irritation test conducted according to FHSA/CPSC Design, 16 CFR 1500 was performed with New Zealand White rabbits (3/group) administered topical applications of 0.5 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (2.5-5% aqueous solutions) to shaved intact or abraded skin under occlusive dressing for 4 hours. An observation period of up to 72 hours followed the exposure period. No edema was observed at either concentration. One animals at 2.5% had evidence of erythema (mean score of 0.5/4 at 24 and 72 hours) while two animals at 5% had evidence of erythema (mean scores of 0.5/4 and 1.5/4 at 24 and 72 hours). The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was not irritating in this study.

- Based on necrosis of the skin being observed in at least one study, ToxServices classified dodecyldimethylamine oxide as a GHS Category 1 dermal irritant.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): vH
Dodecyldimethylamine oxide was assigned a score of Very High for eye irritation/corrosivity based on ToxServices classifying it as a GHS Category 1 eye irritant. GreenScreen® criteria classify chemicals as a Very High hazard for eye irritation/corrosivity when they are classified as GHS Category 1 eye irritants (CPA 2016b). The confidence in the score is high as it is based on data from high quality and/or well-documented studies.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:*
        - New Zealand – GHS – 8.3A - Corrosive to ocular tissue
            - Based on EU R-phrase R34 (Causes burns) listed on any MSDS. No further details were provided.
        - Japan GHS: Serious eye damage/eye irritation – Category 2A
            - Based on severe ocular irritation observed in rabbits. No further details were provided.
- OECD 2006
    - A GLP-compliant ocular irritation test conducted according to the Draize method (low volume procedure) was performed with New Zealand albino rabbits (2 males and 4 females) administered ocular instillations of 10 µL of a hair mousse formulation containing 0.3% dodecyldimethylamine oxide. Eyes were not washed and an observation period of 21 days followed the instillation. All of the eyes showed no signs of irritation after 1 day. The study authors concluded that dodecyldimethylamine oxide was not irritating to the eyes in this study.
    - A GLP-compliant ocular irritation test was conducted according to guideline HSLA 16, 1500.42 and performed in 6 rabbits (sex and species not reported) administered ocular instillations of dodecyldimethylamine oxide (30% purity, balance is water). An observation period of 7 days followed the instillation. The treatment was slightly irritating to the eyes, with clear corneas and irises in all animals, and conjunctival redness and chemosis scores of 0-1. No further details were provided.
    - Three additional ocular irritation studies were identified in the SIDS document. However, they were assigned Klimisch scores of 4 (not assignable). Therefore, ToxServices did not include them in this assessment.
- ECHA 2016
    - A pre-GLP ocular irritant conducted according to OECD TG 405 was performed with New Zealand White rabbits (3/group) administered ocular instillations of 0.1 mL undiluted dodecyldimethylamine oxide (27.8% a.i.). One group of animals did not have their eyes rinsed while the second group had their eyes rinsed 4 seconds after contact with 20 mL lukewarm water. An observation period of 35 days followed the instillation. The group without rinsing exhibited a maximum average score was 4.0 at 1 day, with irreversible corneal opacity in all three animals till 35 days, no iridic response, conjunctival redness with grade 1 fully reversible by 14 days, and conjunctival chemosis up to grade 2 fully reversible by 14 days. The group with rinsing exhibited a maximum average score was 3.67 at day 1, with irreversible corneal opacity in one animal until the end of the observation period, no iridic response, conjunctival redness with grade 1 fully reversible by 14 days, and conjunctival chemosis up to grade 2 fully reversible within 2 days. The study authors concluded that the test material produced irreversible effects to the eyes in this study. [13]

[13] It is not entirely clear if this study was conducted on the target chemical. The ECHA record provided conflicting information on the tested material.

- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - A pre-GLP ocular irritation test conducted according to U.S. Federal Register Vol. 38 (187) 1500:42 (1973) was performed with New Zealand White rabbits (6 unwashed, 3 washed) administered ocular instillations of 0.1 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (6% active solution of a shampoo raw material). The eyes were either unwashed or were washed wish sterile distilled water after 5 seconds of contact with the eyes. An observation period of 7 days followed the instillation. At 24, 48, and 72 hours, the mean corneal score was 1/4, the mean iris score was 0.6/4, the mean conjunctival score was 2.5/4, and the mean chemosis score was 2.2/4. The ocular effects were not fully reversible by the end of the observation period. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was irritating to the eyes in this study.
        - A pre-GLP ocular irritation test conducted according to OECD TG 405 was performed with New Zealand White rabbits (3/sex/group) administered ocular instillations of 0.1 mL amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (28% purity) in water as undiluted or 10% (w/w) solutions in distilled water. Three groups of animals were used: one group (Group 1) of animals were administered instillations of undiluted material without rinsing, the second group (Group 2) was administered instillations of undiluted material with eyes rinsed 4 seconds after contact with 20 mL lukewarm water, and the third group (Group 3) was administered instillations with the 10% (w/w) solution. An observation period of up to 35 days followed the instillation. Irreversible irritation was observed with Groups 1 and 2 while Group 3 recovered fully within 21 days. Group 1 animals exhibited irreversible corneal opacity in all three animals up to day 35, iridic responses of grade 1, conjunctival redness up to grade 2, and chemosis up to grade 3 consisting of swelling with lids about half closed. Group 2 animals exhibited irreversible corneal opacity in one animal till 35 days, iridic response up to grade 1, conjunctival redness up to grade 2.5 with more diffuse beefy red areas, and conjunctival chemosis up to grade 2.5. Group 3 animals exhibited corneal opacity which was reversible within 7 days, iridic response up to grade 1, conjunctival redness up to grade 2 (more diffuse crimson red areas), and conjunctival chemosis up to grade 2. The maximum average scores were 8.0 on the 4^{th} day, 6.0 on the 3^{rd} day, and 4.8 on the 2^{nd} day for Groups 1, 2, and 3, respectively. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides produced irreversible effects to the eyes in this study.

          A non-GLP-compliant ocular irritation study was performed with New Zealand White rabbits (3 total) administered ocular instillations of 0.1 mL undiluted amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (2.5-5% aqueous solution). An observation period of up to 168 hours followed the instillation. The 2.5% solution produced the following scores at 24, 48, and 72 hours: a mean corneal score of 16.1/80, a mean iris score of 5/10, and a mean conjunctival score of 12.8/20. The 5% solution produced the following scores at 24, 48, and 72 hours: a mean corneal score of 19.4/80, a mean iris score of 5/10, and a mean conjunctival score of 13.3/20. The study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was irritating to the eyes in this study.

- Based on the irreversible effects on the eyes observed for dodecyldimethylamine oxide and the analog amines, C12-14 (even numbered)-alkyldimethyl, N-oxides, ToxServices classified dodecyldimethylamine oxide as a GHS Category 1 eye irritant.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): vH
Dodecyldimethylamine oxide was assigned a score of Very High for acute aquatic toxicity based on acute aquatic toxicity values as low as 0.055 mg/L. GreenScreen® criteria classify chemicals as a Very High hazard for acute aquatic toxicity when acute aquatic toxicity values are no greater than 1 mg/L (CPA 2016b). The confidence in the score is high as it is based on data from high quality and/or well-documented studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - Japan – GHS – Hazardous to the aquatic environment (acute) – Category 1
      - Based on an acute aquatic toxicity value of 0.081 mg/L for algae.
    - New Zealand GHS – 9.1A (fish) (GHS Category 1): Very ecotoxic in the aquatic environment
      - Based on bioaccumulation potential.
- ECHA 2016
  - 96-hour LC_{50} (*Danio rerio*, zebrafish) = 31.8 mg/L (non-GLP-compliant, OECD TG 203)
  - 48-hour mobility EC_{50} (*Daphnia magna*) = 3.9 mg/L (GLP-compliant, OECD TG 202)
  - 48-hour EC_{50} (*D. magna*) = 4.24 mg/L (non-GLP-compliant, EU Method C.2)
  - 72-hour EbC_{50} (*Pseudokirchneriella subcapitata*, microalga) = 0.07 mg/L (GLP-compliant, OECD TG 201)
  - 72-hour ErC_{50} (*P. subcapitata*, algae) = 0.20 mg/L (GLP-compliant, OECD TG 201)
- OECD 2006
  - 96-hour LC_{50} (*Oryzias latipes*, Japanese rice fish) = 24.2-41.4 mg/L (GLP-compliant, OECD TG 203)
  - 96-hour LC_{50} (*D. rerio*, zebrafish) = 24-43 mg/L (GLP-compliant, OECD TG 203)
  - 48-hour EC_{50} (*D. magna*) = 3.9 mg/L (GLP-compliant, OECD TG 202)
  - 48-hour EC_{50} (*D. magna*) = 2.23 mg/L (GLP-compliant, OECD TG 202)
  - 48-hour EC_{50} (*D. magna*) = 3.5-5.2 mg/L (non-GLP-compliant, OECD TG 202)
  - 72-hour EbC_{50} (*Scenedesmus subspicatus*, algae) = 0.036 mg/L (GLP-compliant, OECD TG 201)
  - 72-hour ErC_{50} (*S. subspicatus*, algae) = 0.129 mg/L (GLP-compliant, OECD TG 201)
  - 72-hour EbC_{50} (*Selenastrum capricornutum*, algae) = 0.055 mg/L (GLP-compliant, OECD TG 201)
  - 72-hour ErC_{50} (*S. capricornutum*, algae) = 0.11 mg/L (GLP-compliant, OECD TG 201)
  - 72-hour EbC_{50} (*S. capricornutum*, algae) = 0.064 mg/L (non-GLP-compliant, OECD TG 201)
  - 72-hour ErC_{50} (*S. capricornutum*, algae) = 0.204 mg/L (non-GLP-compliant, OECD TG 201)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): vH
Dodecyldimethylamine oxide was assigned a score of Very High for chronic aquatic toxicity based on chronic aquatic toxicity values as low as 0.005 mg/L. GreenScreen® criteria classify chemicals as a

Very High hazard for chronic aquatic toxicity when chronic aquatic toxicity values are no greater than 0.1 mg/L (CPA 2016b). The confidence in the score is high as it is based on data from high quality and/or well-documented studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - 21-day NOEC (*D. magna*) = 0.36 mg/L (GLP-compliant)
  - 72-hour NOEC (*S. subspicatus*, algae) = 0.005 mg/L (GLP-compliant, OECD TG 201)
- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
  - ECHA 2016
    - 15-day survival and mean length NOEC (*Pimephales promelas*, fathead minnow) = 0.495 mg/L (pre-GLP, EPA OPPTS 850.1500)
    - 302-day survival NOEC (*P. promelas*, fathead minnow) = 0.42 mg/L (pre-GLP, EPA OPPTS 850.1500)
    - 21-day reproduction NOEC (*Daphnia magna*) = 0.7 mg/L (pre-GLP, OECD TG 211)

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL

Dodecyldimethylamine oxide was assigned a score of Very Low for persistence based on it meeting the 10-day biodegradation window and the dominant compartment being identified as soil. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when soil is the dominant environmental compartment and the 10-day biodegradation window is met (CPA 2016b). The confidence in the score is high as it is based on data from high quality and/or well-documented studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
  - A GLP-compliant aerobic biodegradability test was conducted according to test procedure reported as "Biodegradation study. Activated sludge simulation test with ^{14}C. Lisec Laboratories, The Netherlands. Protocol # WG-01 ECMETS 537/01" with continuous activated sludge and exposed to ^{14}C-labeled dodecyldimethylamine oxide at concentrations of 110, 384, and 990 µg/L (100% purity) at test periods of 33, 21, and 7 days, respectively. The level of degradation was ≥ 99.9%, ≥ 99.8%, and ≥ 99.9% after exposure to above concentrations and test periods, respectively. The study authors concluded that dodecyldimethylamine oxide was rapidly and ultimately biodegradable in this test.
  - A non-GLP-compliant aerobic test was conducted according to the Effluent in River Die Away Test (Procter & Gamble protocol, study # ECM ETS 553) with activated sludge and exposed to 1 and 2 µg/L of ^{14}C-labeled dodecyldimethylamine oxide (98.6% purity), and after 14 days, 0.78 µg/L and 1 µg/L remained, respectively. The study authors concluded that dodecyldimethylamine oxide was rapidly and ultimately biodegradable in this test.
  - Two additional degradability studies were identified in the SIDS document. However, they were assigned Klimisch scores of 3 (not reliable). Therefore, ToxServices did not include them in this assessment.

- ECHA 2016
    - A non-GLP-compliant ready biodegradability test conducted according to OECD TG 301 B (CO_2 Evolution Test) was performed with non-adapted, activated domestic sludge exposed to dodecyldimethylamine oxide (pure active substance) at 20 mg/L (14.29 mg/L TOC) for 28 days. The degree of degradation was 15.66% after 3 days, 65.88% after 9 days, and 95.27% after 28 days. The 10-day window was met and the study authors concluded that dodecyldimethylamine oxide was readily biodegradable in this study.
    - A GLP-compliant ready biodegradability test conducted according to OECD TG 301 B was performed with activated sludge (adaptation not specified) exposed to dodecyldimethylamine oxide (31% lauryl dimethyl amine oxide in water) at 14.8 mg/L (22.7% TOC) for 28 days. The degree of degradation was 10% after 2 days, 60% after 10 days, and 80% after 28 days. The 10-day window was met and the study authors concluded that dodecyldimethylamine oxide was readily biodegradable in this study.
- Analog: Amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (CAS #N/A, EC Number 931-292-6)
    - ECHA 2016
        - A GLP-compliant ready biodegradability test conducted according to OECD TG 301 D (Closed Bottle test) was performed with activated sludge (adaptation not specified) exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (29.8% amine oxide, 0.4% free amine, 69.98% water) at 6.8 mg/L for 28 days. At the end of the exposure period the level of degradation was 93% and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was readily biodegradable in this test.
        - A pre-GLP ready biodegradability test conducted according to German Standard Method 38 412 was performed with activated sludge (adaptation not specified) exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (purity not specified) at 2 g/L for 28 days. At the end of the exposure period, the level of degradation was 86%. The 10-day window was met and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was readily biodegradable in this test.
        - A non-GLP-compliant ready biodegradability test conducted according to OECD TG 301 B was performed with non-adapted, activated domestic sludge exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (pure active substance) at 20 mg/L (12.39 mg/L TOC) for 28 days. The level of degradation was 14.55% after 3 days, 62.17% after 9 days, and 86.83% after 28 days. The 10-day window was met and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was readily biodegradable in this study.
        - A GLP-compliant ready biodegradability test conducted according to OECD TG 301 B was performed with non-adapted, activated domestic sludge exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (30% diluted) at 73.2 mg/L (10 mg carbon/L) for 28 days. The level of degradation was 6% after 1 day, 42% after 2 days, 72% after 8 days, and 90% after 28 days. The 10-day window was met and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was readily biodegradable in this study.
        - A non-GLP-compliant ready biodegradability test conducted according to OECD TG 301 B was performed with non-adapted, activated domestic sludge exposed to amines, C12-14 (even numbered)-alkyldimethyl, N-oxides (pure active substance) at 20 mg/L (14.75 mg/L TOC) for 28 days. The level of degradation was 14.3% after 3

days, 64.51% after 10 days, and 88.93% after 28 days. The 10-day window was met and the study authors concluded that amines, C12-14 (even numbered)-alkyldimethyl, N-oxides was readily biodegradable in this study

- U.S. EPA 2012
    - The BIOWIN modeling Ready Biodegradable Predictor indicates that dodecyldimethylamine oxide is expected to be readily biodegradable (see Appendix D). Fugacity modeling predicts 81.1% will partition to soil with a half-life of 30 days, 15.2% will partition to water with a half-life of 15 days, and 3.66% will partition to sediment with a half-life of 135 hours.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Dodecyldimethylamine oxide was assigned a score of Very Low for bioaccumulation based on the estimated BCF value of 7.5 and a calculated partition coefficient of 1.85. This is consistent with OECD and HSDB's conclusions about the bioaccumulation potential of the compound. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when BCF values are no greater than 100, and log K_{ow} values are no greater than 4 (CPA 2016b). The confidence in the score is low as it is based on modeling.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2006
    - An accurate experimental determination of the partition coefficient is difficult, if not possible, for surfactants. This is because they tend to accumulate at the interface of octanol and water. Therefore, partition coefficients for these surface active amine oxides are estimated with the measured solubility in octanol and published critical micellar concentration (CMC) in water. CMCs are considered as a conservative measure of water solubility for surfactants.
    - Based on calculated log K_{ow} values less than 2.7 for amine oxides, the bioconcentration factor is estimated to be < 87 for C12-14 amine oxides. Dodecyldimethylamine oxide has a 12-carbon chain. OECD concluded that the bioaccumulation potential of these compounds is low.
- HSDB 2009
    - Potential bioconcentration for aquatic organisms is suggested to be low based on a calculated bioconcentration factor of 0.7.
- U.S. EPA 2012
    - BCFBAF predicts a BCF of 7.524 based on the calculated log K_{ow} of 1.85 for the analog amines, C12-14(even numbered)-alkyldimethyl, N-oxides (CAS #NA, EC #931-292-6) (see Appendix D).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): ***L***
Dodecyldimethylamine oxide was assigned a score of Low for reactivity based on ToxServices not classifying it as a reactive chemical under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classification is available (CPA 2016b). Confidence in this score is low as it is not based on measured data or authoritative listings.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.

  - *Screening:* Not present on any screening lists for this endpoint.
- NITE 2006
  - Not classified as self-reactive, even though similar N-oxide containing chemical groups do have explosive properties. (no other information reported)
  - Not classified as an explosive, even though similar N-oxide containing chemical groups do have explosive properties. The calculated oxygen budget is -296. (No other information reported)
- ACToR 2016
  - Dodecyldimethylamine oxide is stable over an extensive pH range and at high electrolyte concentrations.
- Sigma-Aldrich 2014
  - A material safety data sheet for dodecyldimethylamine oxide states that it has a reactivity rating of 1 from NFPA ("Normally stable, but can become unstable at elevated temperatures and pressures (e.g. propene)") and a physical hazard rating of 1 from HMIS ("Materials that are normally stable but can become unstable (self-react) at high temperatures and pressures. Materials may react non-violently with water or undergo hazardous polymerization in the absence of inhibitors").
- Dodecyldimethylamine oxide does not possess the structural alerts for reactivity identified by the United Nations (2010) in Appendix E.
- Based on the information presented above, ToxServices did not classify dodecyldimethylamine oxide as a reactive chemical under GHS criteria (UN 2015).

Flammability (F) Score (vH, H, M, or L): L

Dodecyldimethylamine oxide was assigned a score of Low for flammability based on ToxServices not classifying it as a flammable chemical under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for flammability when no GHS classification is available (CPA 2016b). Confidence in this score is high as it is based on data from a high quality study.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2016
  - Dodecyldimethylamine oxide was not flammable in a GLP-compliant EU Method A.10 (Flammability (Solids)) test.
- Based on the results of the above test, ToxServices did not classify dodecyldimethylamine oxide as a flammable chemical under GHS criteria (UN 2015).

References

Aggregated Computational Toxicology Resource (ACToR). 2016. Online entry for N,N-Dimethyldodecylamine-N-oxide. Available: http://actor.epa.gov/actor/GenericChemical?casrn=1643-20-5

ChemIDplus. 2016. Entry for Lauramine oxide (CAS #1643-20-5). United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/rn/startswith/1643-20-5

Clean Production Action (CPA). 2016a. The GreenScreen® for Safer Chemicals Chemical Hazard Assessment Guidance. Version 1.3 Guidance. Dated March, 2016. Available at: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2016b. GreenScreen Version 1.3 Hazard Criteria. Dated: March 2016. Available at: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2016c. The GreenScreen® for Safer Chemicals Version 1.3 GreenScreen Benchmarks™. Dated March 2016. Available at: http://www.greenscreenchemicals.org/.

European Chemicals Agency (ECHA). 2016. REACH Dossier for Dodecyldimethylamine oxide (CAS #1643-20-5). Available at: http://echa.europa.eu/registration-dossier/-/registered-dossier/10062/1

Grandjean, P., and P.J. Landrigan. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368: 2167-2178.

Grandjean, P., and P.J. Landrigan. 2014. Neurobehavioral effects of developmental toxicity. The Lancet 13: 330-338.

Hazardous Substances Data Bank (HSDB). 2009. Entry for Lauramine Oxide (CAS #1643-20-5). HSDB Number 5451. Last revision date January 5, 2009. United States National Library of Medicine. Available at: https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+1643-20-5

National Institute of Technology and Evaluation (NITE). 2006. Online record for N,N-Dimethyldodecylamine N-oxide (CAS #1643-20-5). Incorporated Administrative Agency, Governmnet of Japan. Available: http://www.safe.nite.go.jp/english/ghs/06-imcg-0415e.html

Organization for Economic Co-operation and Development (OECD). 2006. SIDS Initial Assessment Profile for Amine Oxides. Available: http://webnet.oecd.org/hpv/ui/SIDS_Details.aspx?id=ef6272f9-0538-4c47-98b1-747ec8ab20b0

Pharos. 2016. Pharos Chemical and Material Library Entry for Dodecyldimethylamine oxide (1643-20-5). Available at: http://www.pharosproject.net/material/.

Sigma-Aldrich. 2014. Safety data sheet for N,N-Dimethyldodecylamine N-oxide (CAS #1643-20-5). Product Number 40234. Version 5.1. Revision date June 27, 2014. Available: http://www.sigmaaldrich.com/catalog/product/sigma/40234?lang=en&region=US

ToxServices. 2013a. SOP 1.37: GreenScreen® Hazard Assessments. Dated: April 24, 2013.

ToxServices. 2013b. SOP 1.69: GreenScreen® Hazard Assessments. Dated: August 17, 2013.

United Nations (UN). 2010. UN Manual of Tests and Criteria. Manual of Tests and Criteria. Revised Fifth Edition. Available: http://www.unece.org/trans/danger/publi/manual/rev5/manrev5-files_e.html.

United Nations (UN). 2015. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Sixth revised edition.

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available at: http://www.gpo.gov/fdsys/pkg/CFR-2008-title49-vol2/pdf/CFR-2008-title49-vol2-sec172-101.pdf.

United States Department of Transportation (U.S. DOT). 2008b. Classification Criteria. 49 CFR § 173. Available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title49/49cfr173_main_02.tpl

United States Environmental Protection Agency (U.S. EPA). 2012. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

United States Environmental Protection Agency (U.S. EPA). 2015. Safer Choice Standard. Available at: http://www2.epa.gov/saferchoice/safer-choice-standard.

United States Environmental Protection Agency (U.S. EPA). 2016. Safer Chemical Ingredients List (SCIL). Available at: http://www2.epa.gov/saferchoice/safer-ingredients.

APPENDIX A: Hazard Benchmark Acronyms
(in 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: Results of Automated GreenScreen® Score Calculation for Dodecyldimethylamine Oxide (1643-20-5)

TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	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
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	**Dodecyldimethylamine oxide**	**1643-20-5**	**L**	**L**	*M*	*M*	DG	**M**	*H*	*M*	*vH*	*M*	**L**	DG	*vH*	**vH**	**vH**	**vH**	**vL**	*vL*	*L*	**L**

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	Yes	Yes	No
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Dodecyldimethylamine oxide	2

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

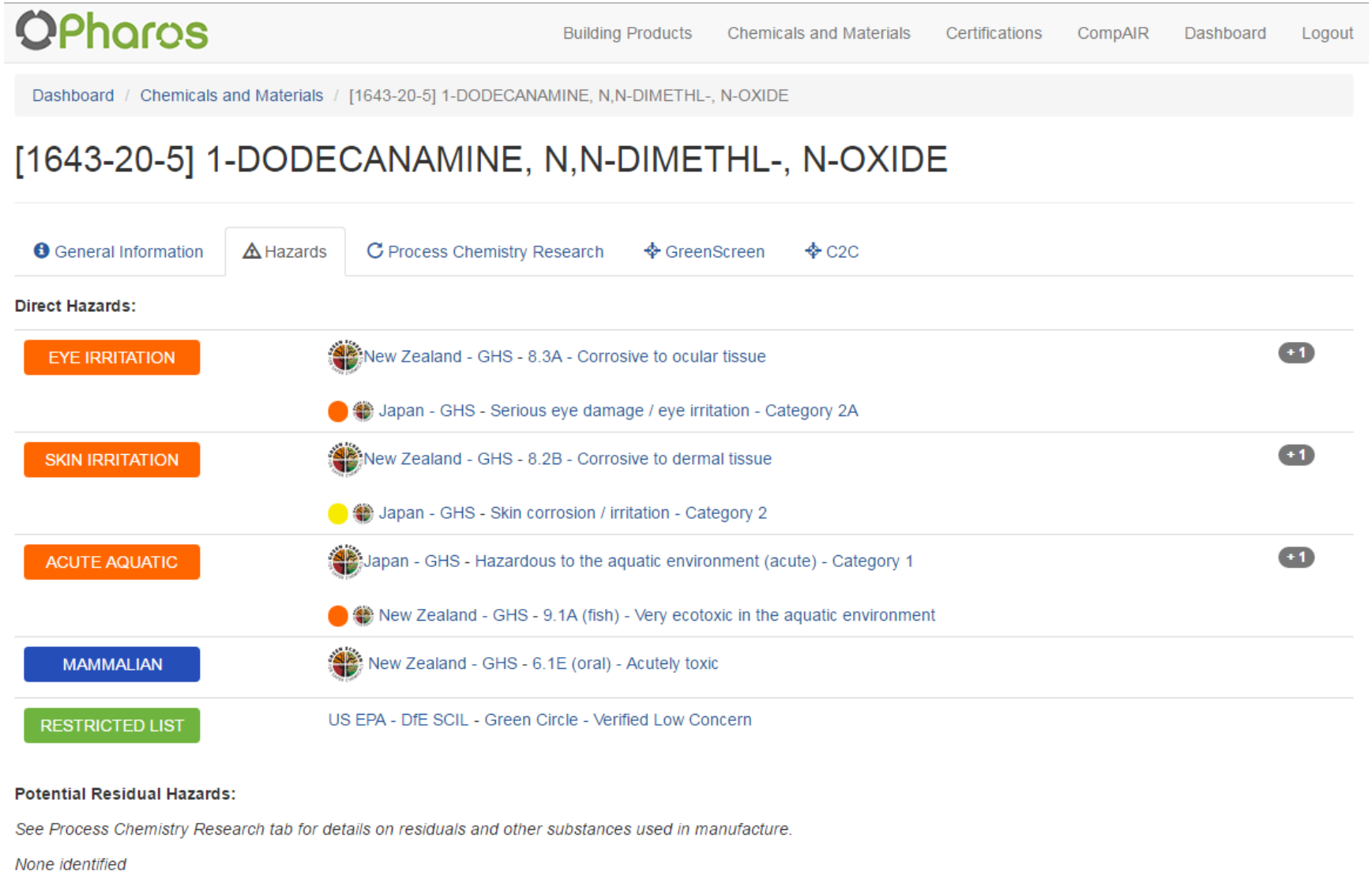
Chemical Name	Final GreenScreen® Benchmark Score
Dodecyldimethylamine oxide	2

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2	Yes	Yes	Yes	Yes	Yes							2
3												
4												

APPENDIX C: Pharos Output for Dodecyldimethylamine Oxide (1643-20-5)



APPENDIX D: EPISuite Modeling Results for Dodecyldimethylamine Oxide (1643-20-5)

CAS Number: 1643-20-5
SMILES : O=N(CCCCCCCCCCCC)(C)C
CHEM : 1-Dodecanamine, N,N-dimethyl-, N-oxide
MOL FOR: C14 H31 N1 O1
MOL WT : 229.41
---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:
Log Kow (octanol-water): 1.85
Boiling Point (deg C) : ------
Melting Point (deg C) : 130.00
Vapor Pressure (mm Hg) : 1.58E-007
Water Solubility (mg/L): 1.9E+005
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.68 estimate) = 4.67

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 426.62 (Adapted Stein & Brown method)
Melting Pt (deg C): 167.95 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 1.65E-007 (Modified Grain method)
VP (Pa, 25 deg C) : 2.2E-005 (Modified Grain method)
MP (exp database): 132-133 deg C
Subcooled liquid VP: 1.73E-006 mm Hg (-999 deg C, user-entered VP)
: 0.00023 Pa (-999 deg C, user-entered VP)

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 390.2
log Kow used: 1.85 (user entered)
melt pt used: 130.00 deg C
Water Sol (Exper. database match) = 1.9e+005 mg/L (25 deg C)
Exper. Ref: BROWN,SL ET AL. (1975C)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 0.054803 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Aliphatic Amines

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 6.61E-011 atm-m3/mole (6.70E-006 Pa-m3/mole)
Group Method: Incomplete
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:

HLC: 2.510E-013 atm-m3/mole (2.543E-008 Pa-m3/mole)
VP: 1.58E-007 mm Hg (source: User-Entered)
WS: 1.9E+005 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: 1.85 (user entered)
Log Kaw used: -8.568 (HenryWin est)
Log Koa (KOAWIN v1.10 estimate): 10.418
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 0.7468
Biowin2 (Non-Linear Model) : 0.8313
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.9905 (weeks)
Biowin4 (Primary Survey Model) : 3.7858 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.5652
Biowin6 (MITI Non-Linear Model): 0.7192
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.1278
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): 0.000231 Pa (1.73E-006 mm Hg)
Log Koa (Koawin est): 10.418
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 0.013
Octanol/air (Koa) model: 0.00643
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 0.32
Mackay model : 0.51
Octanol/air (Koa) model: 0.34

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 27.2472 E-12 cm3/molecule-sec
Half-Life = 0.393 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 4.711 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
0.415 (Junge-Pankow, Mackay avg)
0.34 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 7998 L/kg (MCI method)
Log Koc: 3.903 (MCI method)
Koc : 76.39 L/kg (Kow method)
Log Koc: 1.883 (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 = 0.888 (BCF = 7.72 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -0.5213 days (HL = 0.3011 days)
Log BCF Arnot-Gobas method (upper trophic) = 0.876 (BCF = 7.524)
Log BAF Arnot-Gobas method (upper trophic) = 0.876 (BAF = 7.524)
log Kow used: 1.85 (user entered)

Volatilization from Water:
Henry LC: 2.51E-013 atm-m3/mole (calculated from VP/WS)
Half-Life from Model River: 3.533E+009 hours (1.472E+008 days)
Half-Life from Model Lake : 3.854E+010 hours (1.606E+009 days)

Removal In Wastewater Treatment:
Total removal: 2.13 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 2.03 percent
Total to Air: 0.00 percent
(using 10000 hr Bio P,A,S)

Removal In Wastewater Treatment:
Total removal: 92.29 percent
Total biodegradation: 91.81 percent
Total sludge adsorption: 0.48 percent
Total to Air: 0.00 percent
(using Biowin/EPA draft method)

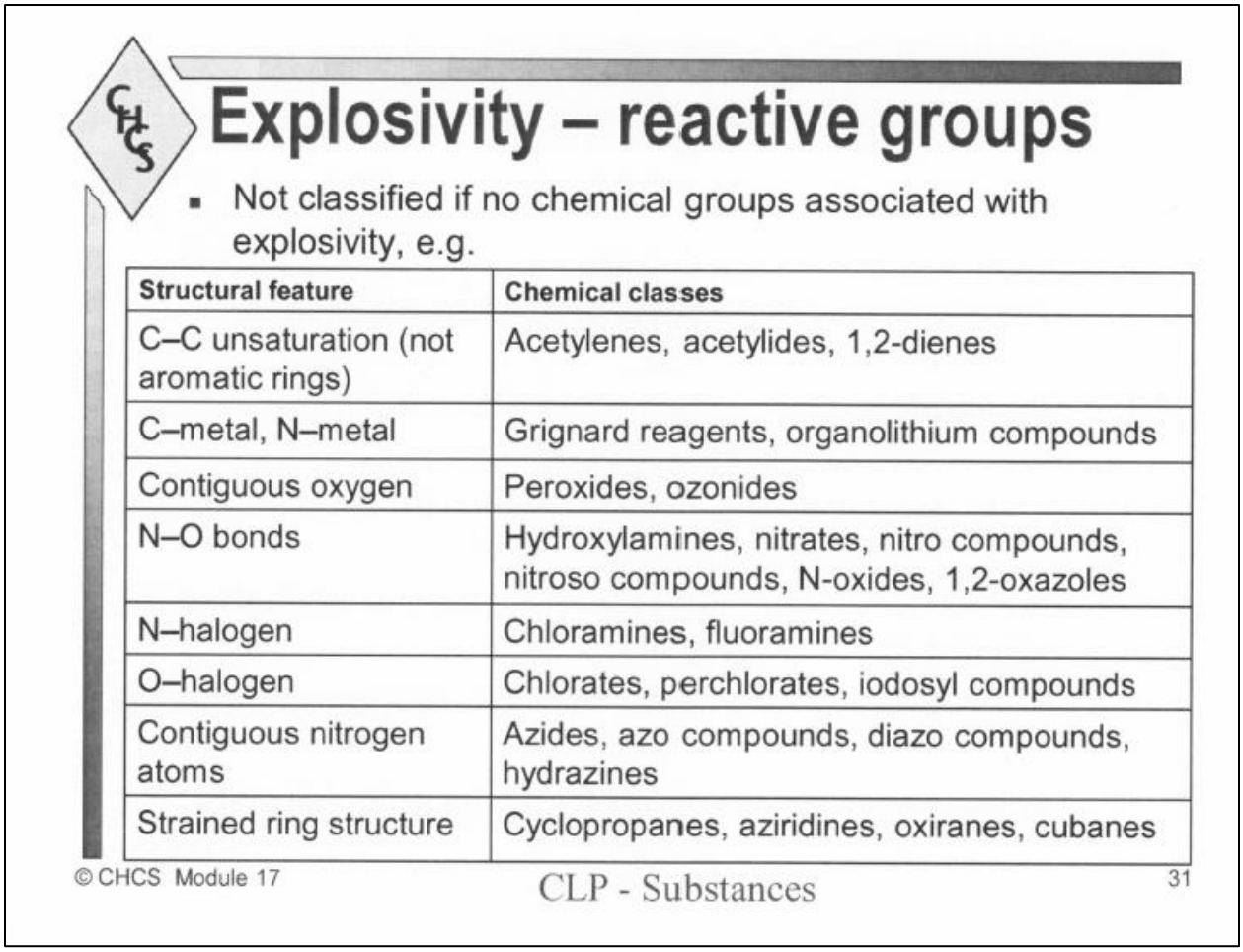
Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	6.43e-006	9.42	1000
Water	15.2	360	1000
Soil	81.1	720	1000
Sediment	3.66	3.24e+003	0

Persistence Time: 810 hr

APPENDIX E: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

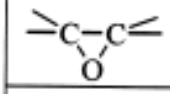
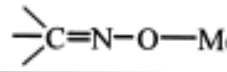
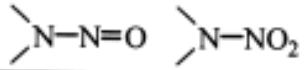
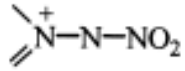
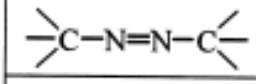
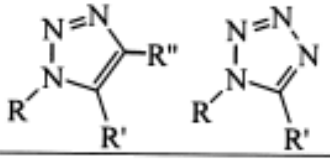
- Not classified if no chemical groups associated with explosivity, e.g.

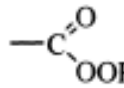
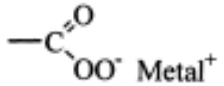
Structural feature	Chemical classes
C–C unsaturation (not aromatic rings)	Acetylenes, acetylides, 1,2-dienes
C–metal, N–metal	Grignard reagents, organolithium compounds
Contiguous oxygen	Peroxides, ozonides
N–O bonds	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N–halogen	Chloramines, fluoramines
O–halogen	Chlorates, perchlorates, iodosyl compounds
Contiguous nitrogen atoms	Azides, azo compounds, diazo compounds, hydrazines
Strained ring structure	Cyclopropanes, aziridines, oxiranes, cubanes

© CHCS Module 17 CLP - Substances 31

Explosivity – Full List

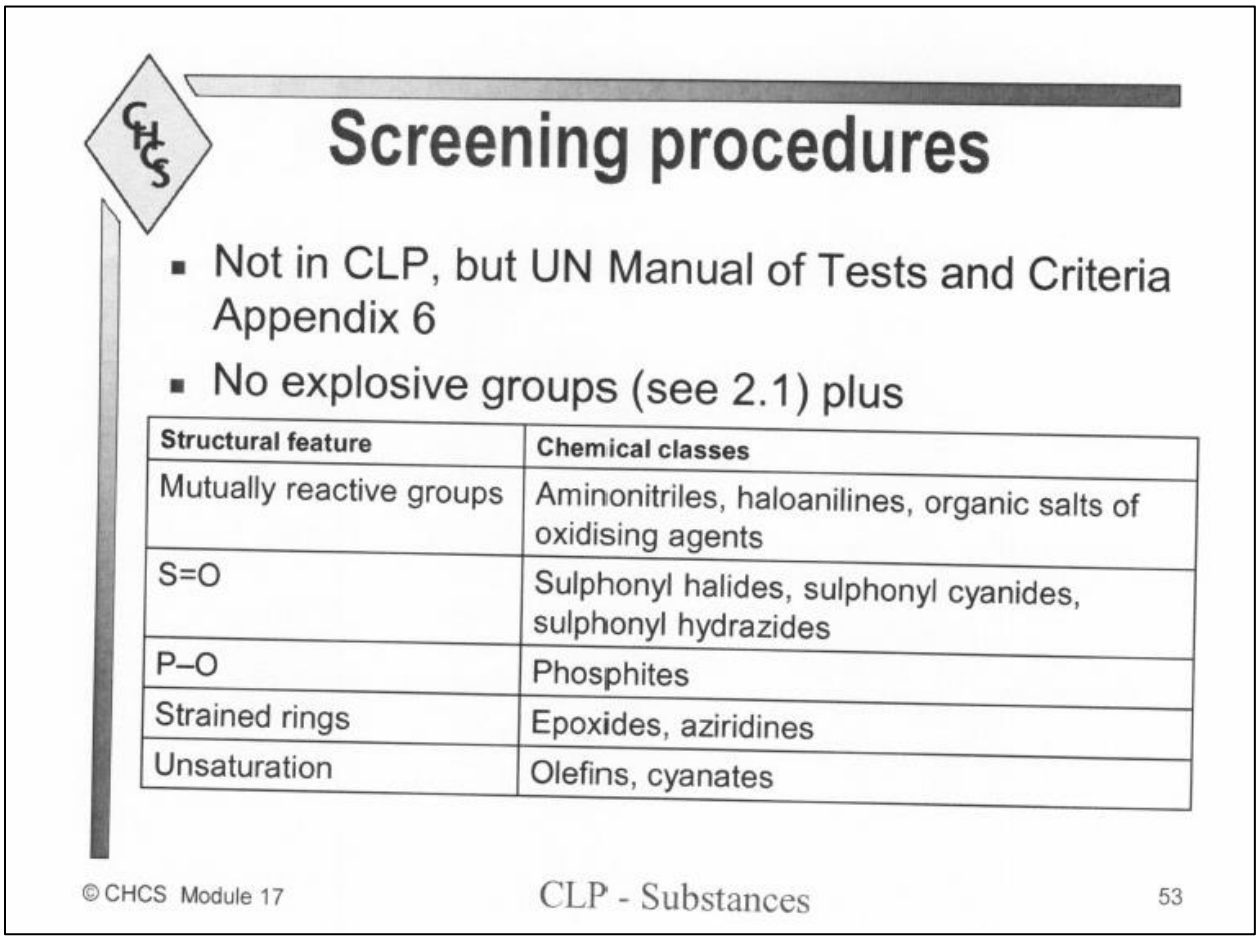
Table R.7.1-28 Chemical groups associated with explosive properties

Chemical group	Chemical Class
-C≡C- -C≡C-Metal -C≡C-Halogen	Acetylenic Compounds Metal Acetylides Haloacetylene Derivatives
	Diazo Compounds
-N=O -NO_2	Nitroso and Nitro Compounds,
R-O-N=O R-O-NO_2	Acyl or Alkyl Nitrites and Nitrates
	1,2-Epoxides
	Metal Fulminates or *aci*-Nitro Salts
	N-Metal Derivatives (especially heavy metals)
	N-Nitroso and N-Nitro Compounds
	N-Azolium Nitroimidates
	Azo Compounds
Ar-N=N-O-Ar	Arene Diazoates
$(ArN=N)_2O$, $(ArN=N)_2S$	Bis-Arenediazo Oxides and Sulfides
RN=N-NR'R''	Triazines
	High-nitrogen Compounds: e.g. Triazoles, Tetrazoles

Chemical group	Chemical Class
[1] ROOR', [2] 	Peroxy Compounds: [1] Alkyl hydroperoxides (R'=H), Peroxides (R'=organic); [2] Peroxo acids (R'=H), Peroxyesters (R'=organic)
[1] ROOMetal, [2] 	Metal peroxides, Peroxoacids salts
$-N_3$	Azides e.g. PbN_6, CH_3N_3
$^{-}O-C-N_2^{+}$	Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide
Ar-N=N-S- Ar-N=N-S-Ar	Diazonium sulfides and derivatives, Arenediazo Aryl Sulfides
XO_n	Halogen Oxide: e.g. percholrates, bromates, etc
NX_3 e.g. $NC1_3$, $RNC1_2$	N-Halogen Compounds

Adapted from Bretherick (Bretherick's Handbook of Reactive Chemical Hazards 6th Ed., 1999, Butterworths, London)

Self-Reactive Substances



Sources to Check for GreenScreen® Hazard Assessment

Note: For a GreenScreen® Hazard Assessment, data queries should be initially limited to the following references. If data gaps exist after these references have been checked, additional references may be utilized.

U.S. EPA High Production Volume Information System (HPVIS): *http://www.epa.gov/hpvis/index.html*.

UNEP OECD Screening Information Datasets (SIDS): *http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html*.

OECD Existing Chemicals Database: *http://webnet.oecd.org/hpv/ui/SponsoredChemicals.aspx*.

European Chemical Substances Information System IUCLID Chemical Data Sheets: *http://esis.jrc.ec.europa.eu/index.php?PGM=dat*.

National Toxicology Program: *http://ntp.niehs.nih.gov/*.

International Agency for the Research on Cancer: *http://monographs.iarc.fr/ENG/Classification/index.php*.

Human and Environmental Risk Assessment (HERA) on ingredients of household cleaning products: *http://www.heraproject.com/RiskAssessment.cfm*.

European Chemicals Agency (ECHA) REACH Dossiers: *http://echa.europa.eu/*.

Licensed GreenScreen® Profilers

Dodecyldimethylamine Oxide GreenScreen® Evaluation Prepared by:

Zach Guerrette, Ph.D., D.A.B.T.
Toxicologist
ToxServices LLC

Dodecyldimethylamine Oxide GreenScreen® Evaluation QC'd by:

Bingxuan Wang, Ph.D., D.A.B.T.
Toxicologist
ToxServices LLC