Undecylenic Acid (CAS #112-38-9) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

Environmental Defense Fund

February 1, 2016
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GreenScreen® Executive Summary for Undecylenic Acid (CAS #112-38-9)

Undecylenic acid functions as a cleansing and emulsifying agent, preservative, and as a surfactant in cosmetic formulations. It is also used as a modifying agent in plasticizers and lubricant additives, as well as a fungistat in humans.

Undecylenic acid 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 2f
  - Very High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))

Data gaps (DG) exist for endocrine activity (E), neurotoxicity (single dose neurotoxicity (Ns) and repeated dose neurotoxicity (Nr*)), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), undecylenic acid meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if undecylenic acid were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical. If it were assigned a High or Very High score of the data gaps Ns, Nr*, or SnR*, it would still be categorized as a Benchmark 2 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 Undecylenic Acid

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>M</td>
<td>R</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>DG</td>
</tr>
</tbody>
</table>

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.
GreenScreen® Assessment for Undecylenic Acid (CAS #112-38-9)

Method Version: GreenScreen® Version 1.2
Assessment Type: Certified

Chemical Name: Undecylenic Acid
CAS Number: 112-38-9

GreenScreen® Assessment Prepared By:
Name: Sara M. Ciotti, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: April 30, 2015
Assessor Type: Licensed GreenScreen® Profiler

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Title: Toxicologist
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Assessor Type: Licensed GreenScreen® Profiler

Name: Jennifer Rutkiewicz, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Update Date: December 4, 2015
Assessor Type: Licensed GreenScreen® Profiler

Also called: 10-Undecenoic acid; Undecenoic acid; Undecyl-10-enoic acid; UNII-K3D86KJ24N (ChemIDplus 2015)

Chemical Structure(s):

Confirm application of the de minimus rule: N/A, (this assessment was conducted for the theoretically pure substance)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
A nearly complete dataset was available for undecylenic acid; however, no measured data were identified for the carcinogenicity endpoint.

1 Use GreenScreen® Assessment Procedure (Guidance) V1.2
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
In the absence of available data for the chemical of interest, ToxServices searched for a suitable analog or class of analogs using guidance in the U.S. EPA’s procedure for identifying analogs (U.S. EPA 2010), ECHA’s read across assessment framework (ECHA 2015a) and OECD’s guidance on grouping of chemicals (OECD 2014a). Resources used for the surrogate search included the ChemIDplus structural similarity search, OECD Toolbox, U.S. EPA’s Analog Identification Methodology (AIM), and U.S. EPA’s Chemical Assessment Clustering Engine (ChemACE). Surrogates were considered to be appropriate if they resemble the target in terms of molecular structure and size, contain a substructure of functional group that may play a critical toxicological role, share similar physicochemical properties (e.g. water solubility, partition coefficient), or have common or similar precursors, metabolites, or breakdown products. Where surrogates are used to fill data gaps or as supporting evidence, the use of a surrogate is clearly indicated for that endpoint.

Undecylenic acid is an eleven carbon unsaturated carboxylic acid. No carcinogenicity data were available for its sodium salt; therefore, data for a C18 unsaturated fatty acid salt, sodium 9-octadecenoate, (Z)- was evaluated. This compound is also a monounsaturated carboxylic acid, but contains an 18 carbon chain rather than an 11 carbon chain. Because sodium 9-octadecenoate, (Z)- is much larger in size than undecylenic acid (C18 vs. C11), it is considered a weak surrogate but it still expected to approximate the toxicity of undecylenic acid due to shared organic functional groups. Data for sodium undecylenate, which is the sodium salt of undecylenic acid, and sodium 9-octadecenoate, (Z)- were also presented in the repeated dose systemic toxicity endpoint. Both acids and the salts are expected to be present as the acid form in the stomach. Because sodium is commonly consumed in the diet, this cation is not expected to contribute to toxicity. Therefore, sodium undecylenate is considered to be a strong surrogate.

Sodium undecylenate (CAS# 3398-33-2)

Sodium 9-octadecenoate, (Z)- (CAS# 143-19-1)

**Identify Applications/Functional Uses:** (EC 2015; Bingham and Cohrssen 2012)
1. Cleansing agent in cosmetic formulations
2. Emulsifying agent in cosmetic formulations
3. Preservative in cosmetic formulations
4. Surfactant in cosmetic formulations
5. Modifying agent in plasticizers and lubricant additives
6. Fungistat in humans
GreenScreen® Summary Rating for Undecylenic Acid: Undecylenic acid was assigned a GreenScreen Benchmark Score™ of 2 (“Use but Search for Safer Substitutes”) (CPA 2014). This score is based on the following hazard score combinations:

- Benchmark 2f
  - Very High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA))

Data gaps (DG) exist for endocrine activity (E), neurotoxicity (single dose neurotoxicity (Ns) and repeated dose neurotoxicity (Nr*)), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), undecylenic acid meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if undecylenic acid were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical. If it were assigned a High or Very High score of the data gaps Ns, Nr*, or SnR*, it would still be categorized as a Benchmark 2 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Undecylenic Acid

<table>
<thead>
<tr>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>C M R D E AT ST N SnS* SnR* IrS IrE AA CA P B Rx F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L L L L DG L L L DG DG M DG H H vH vH vL L L L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Because undecylenic acid is expected to be readily biodegradable, it is not expected to have any relevant transformation products.

Introduction
Undecylenic acid functions as a cleansing and emulsifying agent, preservative, and as a surfactant in cosmetic formulations (EC 2015). It is also used as a modifying agent in plasticizers and lubricant additives, as well as a fungistat in humans (Bingham and Cohrsen 2012).

Undecylenic acid is approved by the U.S. FDA for use as an antifungal in OTC products. In the U.S., OTC antifungal products may contain Undecylenic Acid, Calcium Undecylenate or Zinc Undecylenate, individually or in any ratio that provides a total undecylenate concentration of 10 to

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4 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.

5 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.
25%. Undecylenic acid is listed in Annex V, Section 18 of EC Regulation No. 1223/2009, and is approved for use as a preservative in cosmetics sold in the European Union at a maximum use level of 0.2% (as acid) (EC 2009).

ToxServices assessed undecylenic acid against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices’ SOP 1.37 (GreenScreen® Hazard Assessment) (ToxServices 2013).

Preservative Spectrum of Effect:
As summarized below, undecylenic acid displays good fungistatic activity, but is much less effective against bacteria.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Spectrum of Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive bacteria</td>
<td>Inadequate</td>
<td>Siegert 2014</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td>Inadequate</td>
<td>Siegert 2014</td>
</tr>
<tr>
<td>Yeasts/Molds</td>
<td>Good</td>
<td>Siegert 2014</td>
</tr>
<tr>
<td>Head-space protection</td>
<td>No</td>
<td>Siegert 2014</td>
</tr>
</tbody>
</table>

**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 2012a). Pharos (Pharos 2015) 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) 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 undecylenic acid can be found in Appendix C, and classifications for specific endpoints can be found in the appropriate sections. When a classification from GHS New Zealand was available for any endpoint, it was converted to the harmonized GHS classifications using the “Correlation between GHS and New Zealand HSNO Hazard Classes and Categories” document from the New Zealand Environmental Protection Agency (EPA 2012):

**Mammalian**
- New Zealand HSNO/GHS – 6.1A (dermal) – Acutely toxic
- New Zealand HSNO/GHS – 6.1E (oral) – Acutely toxic

**Eye Irritation**
- New Zealand HSNO/GHS – 6.4A – Irritating to the eye

**Skin Irritation**
- New Zealand HSNO-GHS – 6.3A – Irritating to the skin

**Acute Aquatic**
- New Zealand HSNO/GHS – 9.1D (fish) – Slightly harmful in the aquatic environment or are otherwise designed for biocidal action

**Restricted List**
- German FEA – Substances Hazardous to Waters (VwVwS) – Class 1 Low Hazard to Waters
- Environment Canada – Domestic Substances List – Inherently Toxic to Humans: DSL
- substances that meet human health categorization criteria
Physicochemical Properties of Undecylenic Acid

Undecylenic acid is a white solid at room temperature. It is slightly soluble in water. Its vapor pressure indicates that it exists in the vapor and particulate phase. Its partition coefficient indicates that it may have a slight potential to bioaccumulate.

Table 1: Physical and Chemical Properties of Undecylenic Acid (CAS #112-38-9)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C11-H20-O2</td>
<td>ChemIDplus 2015</td>
</tr>
<tr>
<td>SMILES Notation</td>
<td>C(CCCCC=C)CCCCC(O)=O</td>
<td>ChemIDplus 2015</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>184.277</td>
<td>ChemIDplus 2015</td>
</tr>
<tr>
<td>Physical state</td>
<td>Solid</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Appearance</td>
<td>White solid</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Melting point</td>
<td>21.2 - 26.4°C</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>0.0192 Pa (equivalent to 0.000144 mm Hg)</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Water solubility</td>
<td>38.46 mg/L</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Dissociation constant</td>
<td>4.85 at 60°C</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Density/specific gravity</td>
<td>1.0024 g/cm³</td>
<td>ECHA 2015b</td>
</tr>
<tr>
<td>Partition coefficient</td>
<td>log K_{ow} = 4.0</td>
<td>ECHA 2015b</td>
</tr>
</tbody>
</table>

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

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

Undecylenic acid was assigned a score of Low for carcinogenicity based on negative results in an oral carcinogenicity study of the surrogate sodium 9-octadecenoate, (Z)-, with support from modeling results for undecylenic acid. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative, the chemical contains no structural alerts, and the chemical is not GHS classified (CPA 2012b). Confidence in this score was reduced due to reliance on a weak surrogate and modeling.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

Undecylenic Acid (CAS# 112-38-9)

- OECD 2014b; Toxtree 2014
  - Undecylenic acid contains no structural alerts for genotoxic or non-genotoxic carcinogenicity. See Appendix D for OECD Toolbox (2014) modeling results and Appendix E for Toxtree (2014) modeling results.

Surrogate: Sodium 9-octadecenoate, (Z)- (CAS# 143-19-1)

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6 0.0192 Pa * 0.0075 = 0.000144 mm Hg
7 When original study reports were not available, ToxServices summarized study methodology, results, and study author conclusions as reported in secondary sources. In cases where conclusions were not reported or where ToxServices interpreted the results differently based on the information presented in the study summary, ToxServices’ conclusions are clearly stated.
• HERA 2002
  o Sodium 9-octadecenoate, (Z)- was evaluated in a 2-year oral carcinogenicity study that was conducted in male and female F344 rats. Animals (50/sex/dose) were administered sodium 9-octadecenoate, (Z)- in drinking water at concentrations of 0, 2.5, or 5.0 % for 108 weeks. The only statistically significant difference between treated and control animals was an increase in pancreatic tumors in treated males. Authors noted that the incidence of pancreatic tumors in treated animals was within the normal background level for this strain of rat, and attributed the significant increase to the unusual absence of tumors in the control rats. Based on the weight of evidence, authors concluded that sodium 9-octadecenoate, (Z)- does not induce tumors.

• Based on the weight of evidence, a score of Low was assigned. Data were available only for an 18 carbon monounsaturated carboxylic acid, but this surrogate did not produce any evidence of carcinogenicity in a chronic oral study in rats. Because data were available only for the weak surrogate, ToxServices evaluated the structure for carcinogenicity alerts. A lack of alerts also supports a low potential for carcinogenicity. The compound was not in the domain of VEGA, and modeling could not be performed with OncoLogic because the structure does not fall into the chemical classes included in the program.

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

Undecylenic acid was assigned a score of Low for mutagenicity/genotoxicity based on negative findings in *in vivo* and *in vitro* genotoxicity assays. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative for both chromosomal aberrations and gene mutations, the chemical has no structural alerts, and the chemical is not GHS classified (CPA 2012b). Confidence in the score is high because it is based on several well conducted and reported studies.

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

- **ECHA 2015b**
  - **In vitro**: Undecylenic acid was negative in a GLP-compliant *in vitro* mammalian chromosome aberration test conducted according to OECD Guideline 473 in human lymphocytes. Cells were treated with concentrations of 211.25, 325, and 500 µg/mL undecylenic acid (100.2% purity) with and without metabolic activation. Metabolic activation was achieved using Arochlor-induced rat liver S-9. Treatment did not increase the incidence of chromosomal aberrations. No data were provided regarding cytotoxicity. The study authors concluded undecylenic acid was not clastogenic under the conditions of this assay.
  - **In vitro**: Undecylenic acid was negative in a GLP-compliant Ames assay conducted according to OECD Guideline 471 in *Salmonella typhimurium* strain TA98, TA100, TA1535, TA1537, and TA1538. Bacterial cells were treated with concentrations of 10, 50, 100, 250, 500, and 750 µg/mL (doses selected based on cytotoxicity testing at up to 5,000 µg/mL) undecylenic acid (>99% purity) in the presence and absence of metabolic activation. Metabolic activation was achieved using Arochlor-induced rat liver S-9. Treatment did not alter the incidence of His+ revertant colonies per plate. The study authors concluded that undecylenic acid was not mutagenic under the conditions of this assay.
  - **In vitro**: Undecylenic acid was negative in a GLP-compliant *in vitro* mammalian cell gene mutation assay conducted according to OECD Guideline 476 in Chinese hamster...
lung fibroblasts (V79). Cells were treated with concentrations of 10, 30, 100, 300, 500, or 600 µg/mL undecylenic acid (>99% purity) in the presence and absence of metabolic activation. Metabolic activation was achieved using Arochlor-induced rat liver S-9. Treatment did not alter the mutation frequency. The study authors concluded that undecylenic acid was not mutagenic under the conditions of this assay.

- In vitro: Undecylenic acid was negative in a GLP-compliant DNA damage and repair assay (unscheduled DNA synthesis-UDS) conducted according to OECD Guideline 422 in rat hepatocytes. The study authors conducted two tests; cells were treated with 0, 1, 5, 10, 25, 50, and 100 µg/mL undecylenic acid in the first test, and 0, 1, 10, 25, 50, and 100 µg/mL undecylenic acid (100.2% purity) in the second test. Cytotoxicity was seen at concentrations ≥ 100 µg/mL in the preliminary study that tested concentration up to 500 µg/mL. Treatment did not alter thymidine-uptake. The study authors concluded that undecylenic acid was not genotoxic under the conditions of this assay.

- In vivo: Undecylenic acid was negative in a GLP-compliant in vivo mouse micronucleus assay conducted according to OECD Guideline 474 using male and female CD-1 mice. Mice (15/sex/dose) received a single dose of 1,000, 2,000, or 4,000 mg/kg undecylenic acid (purity not reported) via oral gavage and bone marrow was collected 24 or 48 hours after treatment. No clinical signs were reported but three high-dose male mice were found dead 24 or 72 hours after treatment. Treatment did not increase the incidence of polychromatic erythrocytes. The study authors concluded that undecylenic acid was not genotoxic under the conditions of this study.

- Based on the weight of evidence, a score of Low was assigned. Negative results were found in a GLP-compliant in vivo mouse micronucleus assay conducted according to OECD Guideline 474 using male and female CD-1 mice. Negative findings were also observed in in vitro mutagenicity assays using mammalian and bacterial cells, an in vitro chromosome aberration assay, and an in vitro DNA damage and repair assay. The data indicate that undecylenic acid is not genotoxic; therefore, a score of Low was assigned.

**Reproductive Toxicity (R) Score (H, M, or L): L**

Undecylenic acid was assigned a score of Low for reproductive toxicity based on the absence of reproductive toxicity in a GLP-compliant reproductive and developmental screening test. Confidence in this endpoint was reduced due to the reliance on a reproductive toxicity screening test which evaluated limited reproductive endpoints. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative, the chemical has no structural alerts, and the chemical is not GHS classified (CPA 2012b).

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
- ECHA 2015b
  - In a GLP-compliant reproduction and developmental screening test conducted according to OECD Guideline 421, male and female Sprague-Dawley rats received 50, 150, or 450 mg/kg undecylenic acid (98.79% purity) via oral gavage for 2 weeks before mating, during the mating period (2 weeks), and until sacrifice in males, or throughout pregnancy and lactation, until day 4 post-partum in females. Animals were treated once per day, 7 days per week. Parental animals were evaluated daily for clinical signs and body weights were evaluated throughout treatment. Upon completion of the treatment period a gross necropsy and histopathological exam was performed, and reproductive organs were weighted. Treatment had no effect on male or female reproductive performance, or
reproductive organ weight. Histopathological examination found no treatment-related effects. The study authors identified a reproductive NOAEL of 450 mg/kg/day (highest dose tested), based on the absence of adverse effects.

**Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L**

Undecylenic acid was assigned a score of Low for developmental toxicity based on the absence of adverse developmental effects in rats in three independent studies. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data are available and negative, the chemical has no structural alerts, and the chemical is not GHS classified (CPA 2012b). Confidence in the score is high because it is based on a well conducted prenatal developmental toxicity study with support from a screening study.

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

- ECHA 2015b
  - In a GLP-compliant prenatal developmental toxicity study conducted according to OECD Guideline 414, Sprague-Dawley rats (24/dose) received 150 or 450 mg/kg undecylenic acid (98.75% purity) via oral gavage on gestation days 6 through 20. Animals (number of animals not reported) were monitored daily for clinical signs and food consumption. Body weight was monitored throughout the treatment period. Dams were sacrificed on gestation day 21, and the total number of live and dead fetuses, as well as average fetal body weight was recorded. External examinations were performed on all pups, and soft tissue, skeletal, and head examinations were performed on half of each litter. Maternal toxicity was seen in the high dose animals. One pup in the low dose group had several malformations; however, the authors considered them to be of spontaneous origin. No treatment-related effects were found in the fetuses. The study authors identified a developmental NOAEL of 450 mg/kg/day (highest dose tested), based on the absence of adverse developmental effects.
  - In a dose-range study for the previously described prenatal developmental toxicity study, Sprague-Dawley rats (7/dose) received 150, 450, or 1,000 mg/kg undecylenic acid (purity not reported) via oral gavage on gestation days 6 through 19. On day 21 the authors evaluated the number and distribution of dead and live fetuses, fetal body weight, sex distribution, and performed a gross examination. Maternal toxicity was observed at 1,000 mg/kg/day. No adverse developmental effects were reported. The authors identified a developmental NOAEL of 1,000 mg/kg/day (highest dose tested), based on the absence of adverse developmental effects.
  - In the previously described GLP-compliant reproduction and developmental screening test conducted according to OECD Guideline 421, male and female Sprague-Dawley rats received 50, 150, or 450 mg/kg undecylenic acid (98.79% purity) via oral gavage for 2 weeks before mating, during the mating period (2 weeks), and until sacrifice in males, or throughout pregnancy and lactation, until day 4 post-partum in females. Animals were treated once per day, 7 days per week. The study authors evaluated the number and sex of pups, stillbirths, live births, postnatal mortality, presence of gross anomalies, weight gain, and physical and behavioral abnormalities. All pups were examined for external and internal abnormalities. No adverse developmental effects were reported. ToxServices identified a developmental NOAEL of 450 mg/kg/day (highest dose tested), based on the absence of adverse effects.
Endocrine Activity (E) Score (H, M, or L): DG
Undecylenic acid was assigned a score of Data Gap for endocrine activity based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
- 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.

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): L
Undecylenic acid was assigned a score of Low for acute toxicity based on oral LD_{50} values > 2,000 mg/kg in rats and mice and dermal LD_{50} values > 2,000 mg/kg in rats and > 5,000 mg/kg in mice. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are greater than 2,000 mg/kg (CPA 2012b). Confidence in this endpoint was reduced due the lack of conformity between the rat, mouse, and guinea pig dermal studies.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: New Zealand HSNO/GHS – 6.1A (dermal) – Acutely toxic – GHS Category 1
    - Classification is based on the LD_{50} of 50 mg/kg in guinea pigs (EPA 2015)
  - Screening: New Zealand HSNO/GHS – 6.1E (oral) – Acutely toxic – GHS Category 5
    - Classification is based on the LD_{50} of 2,500 mg/kg in rats (EPA 2015)
- ECHA 2015b
  - Oral: LD_{50} = > 2,000 mg/kg in male and female Sprague-Dawley rats (GLP, OECD 401)
  - Dermal: LD_{50} = > 2,000 mg/kg in male and female Sprague-Dawley rats (GLP, OECD 402)
- Bingham and Cohrssen 2012
  - Oral: LD_{50} > 3,200 – 8,150 mg/kg in mice (Eastman Kodak Co. 1980; Tislow et al. 1950)
  - Oral: LD_{50} > 2,500 mg/kg in rats (Eastman Kodak Co. 1980; Frear 1969)
  - Dermal: LD_{50} 50-240 mg/kg in guinea pigs (Eastman Kodak Co. 1980)
- EC 1987
  - Oral: LD_{50} = 2.5-10 g/kg in rats
  - Oral: LD_{50} = 2.3-8.5 g/kg in mice
  - Dermal LD_{50} = > 5,000 mg/kg in rabbits
- Based on the weight of evidence, a score of Low was assigned. Studies conducted according to OECD and GLP standards identified oral and dermal LD_{50} values > 2,000 mg/kg undecylenic acid for rats (ECHA 2015b). Data from an unpublished study report (Eastman Kodak Co. 1980, as cited in Bingham and Cohrssen 2012) identified dermal LD_{50} values ranging from 50 to 240 mg/kg in guinea pigs; however, no details regarding the study design or animal treatment were
GHS-New Zealand classified undecylenic acid as a GHS Category 1 dermal toxicant based on the LD$_{50}$ of 50 mg/kg in guinea pigs. Reported dermal LD$_{50}$ values in other species were much higher, at > 2,000 mg/kg in rats and > 5,000 mg/kg in mice. ToxServices placed low confidence in the guinea pig LD$_{50}$ values because no study details were provided and there is uncertainty regarding the study design and treatment of animals (i.e., condition of the application site (abraded/scarified vs. intact), duration of exposure, and covering of the application (occlusive vs. non-occlusive)). ToxServices acknowledges that guinea pigs may be the most sensitive to undecylenic acid, but no conclusions can be made based on the available data due to the lack of experimental details. Therefore, the weight of evidence indicates a low order of acute toxicity and a score of Low was assigned based on oral LD$_{50}$ values > 2,000 mg/kg for rats from studies conducted according to OECD and GLP standards and dermal LD$_{50}$ values > 2,000 mg/kg in rats and mice. Confidence in this endpoint was reduced due the lack of conformity between the rat, mouse, and guinea pig dermal studies.

**Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)**

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

Undecylenic acid was assigned a score of Low for systemic toxicity (single dose) based on a lack of adverse systemic effects in acute oral and dermal toxicity studies in rats. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when adequate data are available and negative for systemic effects below the guidance value of 2,000 mg/kg for acute oral and dermal studies, the chemical has no structural alerts, and the chemical is not GHS classified (CPA 2012b). Confidence in the score is high because it is based on experimental data from well conducted and reported studies.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- ECHA 2015b
  - Oral: In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401, male and female Sprague-Dawley rats received a single oral dose of 2,000 mg/kg undecylenic acid (99.4% purity). Rats (5/sex) were observed daily for clinical signs and mortality and on day 15 animals were evaluated for changes in gross pathology. Animal body weights were recorded on days 1, 8, and 15. Treatment caused no mortality, significant reductions in body weight, or changes in gross pathology. The authors identified an oral LD$_{50}$ of > 2,000 mg/kg.
  - Dermal: In a GLP-compliant acute dermal toxicity study conducted according to OECD Guideline 402, male and female Sprague-Dawley rats were dermally administered a single dose of 2,000 mg/kg undecylenic acid (99.4% purity) under semi-occlusive conditions for 24 hours. Rats (5/sex) were observed daily for clinical signs, body weight changes, and mortality. Authors performed a necropsy on day 15 and evaluated animals for changes in gross pathology. Treatment caused no mortality, clinical signs, reduction of body weight, or gross pathological changes. The authors identified a dermal LD$_{50}$ of > 2,000 mg/kg.

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

Undecylenic acid was assigned a score of Low for systemic toxicity (repeated dose) based on an oral NOAEL values ≥ 400 mg/kg from studies using undecylenic acid and the surrogates sodium 9-octadecenoate, (Z)- and sodium undecylenate. GreenScreen® criteria classify chemicals as a Low
hazard for systemic toxicity (repeated dose) when the oral NOAEL is greater than 100 mg/kg/day (CPA 2012b).

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

### Undecylenic Acid (CAS# 112-38-9)

- **Bingham and Cohrssen 2012; ECHA 2015b**
  - **Oral**: In a subchronic oral toxicity study, rats were exposed to 100, 200, or 400 mg/kg undecylenic acid (purity not reported) in the diet for periods of 6 to 9 months. Treatment caused no clinical signs, change in animal body weight, or abnormalities (Tislow et al. 1950). No further details were provided. ToxServices identified a NOAEL of 400 mg/kg/day (highest dose tested). *This study was assigned a Klimisch score of 4 (not assignable) in the ECHA REACH Dossier (ECHA 2015b) because only a study abstract was available for review. However, the original study was reviewed and summarized by Bingham and Cohrssen (2012).*

- **ECHA 2015b**
  - In a GLP-compliant reproduction and developmental screening test conducted according to OECD Guideline 421, male and female Sprague-Dawley rats received 50, 150, or 450 mg/kg undecylenic acid (98.79% purity) via oral gavage for 2 weeks before mating, during the mating period (2 weeks), and until sacrifice in males, or throughout pregnancy and lactation, until day 4 post-partum in females (approximately 28 days in males and 53 days in females). Animals were treated once per day, 7 days per week. Parental animals were evaluated daily for clinical signs and body weights were evaluated throughout treatment. Upon completion of the treatment period a gross necropsy and histopathological exam was performed, and reproductive organs were weighted. Two high dose males died on days 3 and 35. No cause of death was found following macroscopic examination. Hypersalivation was observed in males and females treated with 150 mg/kg/day and to a lesser extent in animals treated with 50 mg/kg/day. One male treated with 150 mg/kg/day had transient loud breathing. Treatment had no effect on parental body weight or food consumption. No gross pathological changes were found. Authors of the REACH Dossier identified a systemic NOAEL of 150 mg/kg/day and a LOAEL of 450 mg/kg/day based on the spontaneous death of two high dose male rats. *GHS Guidance values are based on 90-day studies. Therefore, they were multiplied by 3 in order to account for study duration in male rats (most conservative estimate) (i.e., 10-100 mg/kg/day adjusted to 30-300 mg/kg/day). Therefore the LOAEL of 450 mg/kg/day undecylenic acid is greater than the guidance value of 300 mg/kg/day.*

### Surrogate: Sodium 9-octadecenoate, (Z)- (CAS# 143-19-1)

- **HERA 2002**
  - **Oral**: Sodium 9-octadecenoate, (Z)- was evaluated in a 2-year chronic study in male and female F344 rats that was described above for carcinogenicity. Animals (50/sex/dose) were administered sodium 9-octadecenoate, (Z)- in drinking water at concentrations of 0, 2.5, or 5.0 % (approximately 0, 3,225, or 6,450 mg/kg/day for males and 0, 3,600, or 7,200 mg/kg/day for females6) for 108 weeks. There was a slight reduction in body weight gain in males (magnitude and significance not reported). In the clinical chemistry, hematology, and urinalysis evaluations, the only statistically significant

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8 Males: 2.5% = 25,000 mg/L water x 0.129 L water/kg BW/day = 3,225 mg/kg/day; Females: 2.5% = 25,000 mg/L water x 0.144 L water/kg BW/day = 3,600 mg/kg/day (male and female water factor values for Fischer 344 rat chronic study from [http://www.tera.org/Tools/ratmousevalues.pdf](http://www.tera.org/Tools/ratmousevalues.pdf)).
finding was a slight decrease in serum bilirubin in males at the high dose. At the high
dose, there were significant decreases in the mean weights of the liver in males and the
heart, pancreas, and adrenals in females. The weight of the thymus was significantly
increased in females at this dose. The magnitude of change was not specified. The
discussion of histopathological effects was limited to the evaluation of neoplasms
described above for carcinogenicity. ToxServices identified a conservative NOAEL of
3,225 mg/kg/day in males and 3,600 mg/kg/day in females based on effects on organ
weights at the high dose.

**Surrogate:** Sodium Undecylenate (CAS# 3398-33-2)

- **ECHA 2015b**
  - *Oral:* In a GLP-compliant subchronic study conducted according to OECD Guideline
    408, male and female Sprague-Dawley rats (10/sex/dose) received oral doses of 20, 60,
    and 180 mg/kg via oral gavage for 13 weeks. The high dose was increased from 180
    mg/kg to 360 mg/kg on treatment day 51. Animals received half of the dose twice per
day, with approximately 3-4 hours in between doses. An additional 10 animals per sex
were added to the control and high dose group for a 4 week recovery period. Animals
were evaluated for mortality, clinical signs, food and water consumption, food efficiency,
and body weight gain throughout the study. Upon completion of the study, hematology
and clinical chemistry were performed. Animals were also subjected to a macroscopic
and microscopic pathological investigation. Treatment caused no mortality. A dose-
dependent increase in clinical signs was observed. Clinical signs included excessive
salivation, loud breathing/respiratory difficulties, and poor clinical conditions. Food
consumption and body weight were reduced in high-dose male rats. The study authors
noted that these effects were more pronounced after the dose increase from 180 mg/kg to
360 mg/kg. Glucose plasma levels and triglyceride levels were decreased in high dose
females. Effects on glucose plasma levels were reversible and were not present after the
4 week recovery period; however, triglyceride levels were still decreased after the
recovery period. Histopathological examination found cardiomyopathy (myocardial
degeneration/monocellular aggregation) in some of the high dose animals (control: 2/20,
This effect was reversible and was not present after the recovery period. Forestomach
oedema/inflammatory cell infiltration was seen in high-dose animals. No treatment-
related effects were seen in the mid and low dose. The study authors identified a
NOAEL of 60 mg/kg/day and a LOAEL of 180/360 mg/kg/day based on clinical signs,
body weight, and clinical chemistry.

- Based on the weight of evidence, a score of Low was assigned. Four repeated dose oral toxicity
studies were identified for this endpoint. In the first study, rats were exposed to undecylenic acid
in their diet for 90 days and a NOAEL of 400 mg/kg/day (highest dose tested) was identified. In
the second study, rats were administered undecylenic acid via oral gavage for 2 weeks before
mating, during the mating period (2 weeks), and until sacrifice in males, or throughout pregnancy
and lactation, until day 4 post-partum in females (approximately 28 days in males and 53 days in
females). The LOAEL was 450 mg/kg/day based on the deaths of two male animals, although
there were no apparent signs of systemic toxicity in these animals. Because limited details were
available in the first study and the second study was of limited duration, and evaluated limited
endpoints, ToxServices also evaluated available surrogate data. In the third study, rats were
exposed to the surrogate sodium 9-octadecenoate, (Z)- in their drinking water for two years and
NOAEL values of 3,225 mg/kg/day in males and 3,600 mg/kg/day in females were identified. In
the fourth study, rats were administered the surrogate sodium undecylenate via oral gavage and
the authors identified a NOAEL of 60 mg/kg/day and a LOAEL of 180/360 mg/kg/day based on clinical signs, body weight, and clinical chemistry. This study involved rats that were administered a dose of 180 mg/kg/day for the first 50 days of treatment followed by a dose of 360 mg/kg/day after day 50. Because the dose increased in the middle of the study, and specific details were not provided on the time-course and severity of effects, it is impossible to discern if the adverse effects would have occurred if the dose was maintained at 180 mg/kg/day (i.e. it is possible that 180 mg/kg/day would have been a NOAEL if the dose had not been increased). The study authors indicated that the changes in body weight were more pronounced after the increase in dose; however, no details were provided on the changes in clinical signs throughout the study. Additionally, the toxicological relevance of changes in clinical signs and clinical chemistry is unclear. Although plasma triglyceride levels were reduced after the recovery period, the authors found no changes in organ weights and no treatment-related histopathological changes to the liver. As these effects are of uncertain toxicological relevance and occurred above the guidance value of 100 mg/kg/day, these changes were not considered to be sufficient to warrant classification for systemic toxicity. Collectively, studies of undecylenic acid and the surrogates indicate that any potential systemic effects occur at doses greater than the guidance values. Therefore, ToxServices assigned a score of Low.

Neurotoxicity (N)

Group II Score (single dose) (vH, H, M, or L): DG
Undecylenic acid was assigned a score of Data Gap for neurotoxicity (single dose) due to insufficient data for this endpoint.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- ECHA 2015b
  - Oral: In a previously described GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401, male and female Sprague-Dawley rats received a single oral dose of 2,000 mg/kg undecylenic acid (99.4% purity). Rats (5/sex) were observed daily for clinical signs and mortality, on day 15 animals were evaluated for changes in gross pathology. On day 1, hypoactivity and piloerection were observed in one male and one female; no effects were seen in the other animals.

  - Based on the weight of evidence, a score of Data Gap was assigned. Oral exposure to a single dose of 2,000 mg/kg undecylenic acid caused hypoactivity and piloerection on day 1 in 20% (2/10) of the tested animals. Because this response was seen in only a small number of treated animals and is commonly observed following gavage administration of a test substance in acute oral studies, and it was only observed on day one, ToxServices did not consider these effects to be indicative of neurotoxicity. ToxServices considered the remaining data to be insufficient for the assignment of a score, as there were no evaluations of neurotoxicity endpoints.

Group II* Score (repeated dose) (H, M, or L): DG
Undecylenic acid was assigned a score of Data Gap for neurotoxicity (repeated dose) based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- No data were identified.
Skin Sensitization (SnS) Group II* Score (H, M, or L): M
Undecylenic acid was assigned a score of Moderate for skin sensitization based on the findings of a mouse local lymph node assay. Confidence in the score is reduced due to conflicting results between the LLNA and sensitization tests in guinea pigs and humans. GreenScreen® criteria classify chemicals as a Moderate hazard for skin sensitization when the chemical is classified as GHS Category 1B (skin sensitizer) (CPA 2012b).
- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
- NTP 2010
  - Undecylenic acid was a weak skin sensitizer in a mouse LLNA assay. Stimulation indices of 2.5, 3.3, and 4.4 were reported for 10%, 25%, and 50% undecylenic acid, respectively. An EC3 value of 19.4 was reported. No further details were provided.
- Bingham and Cohrsen 2012
  - Undecylenic acid was not sensitizing to guinea pigs in a sensitization study. Guinea pigs were topically challenged with undecylenic acid 1 week after an initial footpad injection, and no positive reactions were observed. No further details were provided.
- EC 1987
  - In a maximization test in 25 human volunteers, there were no sensitization responses to a 4% solution in Vaseline. No additional details were provided.
- Based on the weight of evidence, a score of Moderate was assigned. Although undecylenic acid was negative for sensitization in guinea pigs and humans tested with a 4% solution, it was weakly positive in a mouse LLNA. GHS guidance specifies that chemicals with EC3 values > 2% should be classified as GHS Category 1B skin sensitizers. Confidence in this score is reduced due to conflicting results between studies.

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG
Undecylenic acid 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 on any authoritative lists
  - Screening: not on any screening lists
- No data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): H
Undecylenic acid was assigned a score of High for skin irritation/corrosivity based on the results of an acute irritation study conducted according to OECD Guideline 404 which found mild skin irritation that did not resolve within 7 days in rabbits. Confidence in the score is reduced because observations were not conducted up to day 14. GreenScreen® criteria classify chemicals as a High hazard for skin irritation/corrosivity when the chemical is classified as GHS Category 2 (CPA 2012b).
- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: New Zealand HSNO/GHS: 6.3A – Irritating to the skin – GHS Category 2
    - Classification is based on a report of severe skin irritation in rabbits and an R phrase (R38) listed on an MSDS (EPA 2015)
- ECHA 2015b
  - In an acute skin irritation study conducted according to OECD Guideline 404, undiluted...
undecylenic acid (0.5 mL) (98.8% purity) was applied to the skin of rabbits (strain not reported) (n=4) for 4 hours. The type of coverage (i.e., occlusive, semi-occlusive, or non-occlusive) was not reported. Animals were observed for up to 7 days. Treatment produced erythema and edema with individual mean scores (average at 24, 48, and 72 hours) of 1.7, 2, 2, and 1.7 for erythema (mean = 1.85) and 0.5, 0.7, 0.5, and 0.2 for edema (mean = 0.48). Edema resolved within 7 days; however, erythema was not fully reversible within 7 days for 3/4 animals. The ECHA REACH Dossier reported a mean erythema score of 2.35 and classified undecylenic acid as a Category 2 skin irritant. Based on the reported individual mean scores of 1.7, 2, 2, and 1.7, the mean erythema score is 1.85 with none of the scores exceeding 2.3, and undecylenic acid should be classified as Category 3 skin irritant based on mean scores of ≥ 1.5 and < 2.3. However, observations were not conducted up to day 14 to determine reversibility.

- In an acute skin irritation study conducted according to OECD Guideline 404, concentrations of 10 to 80% undecylenic acid (w/v) in ethanol were applied to closely clipped skin of New Zealand White rabbits (sex not reported, n=4) for 24 hours. The study summary does not specify if treatment in rabbits occurred under occlusive or non-occlusive conditions. Animals were observed for 48 hours. Treatment produced mild irritation in rabbits, a mean irritation score of 1.6 (max score = 8, Draize test) was reported. No further details were provided.

- ECHA 2015b; Bingham and Cohrssen 2012
  - In a 21-day continuous patch test, humans (n=4) were exposed to concentrations of 10%, 20%, 40%, or 80% undecylenic acid (w/v) in ethanol under occlusive or non-occlusive conditions. Exposure produced irritation under occlusive conditions, but it was not irritating under non-occlusive conditions. The ECHA REACH Dossier reports an overall irritation score (mean of 4 humans) of 0 at 24 and 72 hours, and cumulative irritation scores (mean of 2 humans) of 38.5, 50.5, and 69 (max score = 84) for 10%, 20%, and 40% undecylenic acid on day 21, respectively. The Dossier did not indicate if the reported scores were for occlusive or non-occlusive treatments. No further details were provided.

- EC 1987
  - Undecylenic acid was extremely irritating when applied to the intact or abraded skin of rabbits for 24 hours. A 30% solution in ethanol was mildly irritating. No additional details were provided.

- Bingham and Cohrssen 2012
  - In an acute skin irritation study, undecylenic acid was applied to depilated guinea pig abdomen for 24 hours under occlusion. Treatment produced moderate skin irritation. No further details were provided (Eastman Kodak Co. 1980).

- ECHA 2015c
  - Undecylenic acid was self-classified with the H-Statement H315 (Causes skin irritation) by 1,079/1,079 notifiers to REACH (notified classification-non-harmonized).

- Based on the weight of evidence, a score of High was assigned. GHS-New Zealand classified undecylenic acid as a GHS Category 2 skin irritant based on a report of severe skin irritation in rabbits and an R-phrase included on an MSDS. GHS-New Zealand (EPA 2015) did not cite the study which found severe skin irritation in rabbits. Acute exposure to undecylenic acid produced erythema and edema in rabbits with scores ranging from 1.7 - 2 and 0.2 - 0.7 in all animals, respectively. GHS Guidance indicates that substances which produce mean scores of ≥ 1.5 and < 2.3 for erythema/eschar or for edema from gradings in at least 2 of 3 tested animals from grades at 24, 48, and 72 hours should be classified as a Category 3 skin irritant (UN 2013). However,
effects did not resolve by day 7 and observations were not conducted up to day 14. Furthermore, because scores at day 7 were not reported, it is not possible to determine the severity of irritation at this time in order to predict whether effects would have resolved by day 14. Therefore, it is possible that GHS Category 2 classification, which applies to chemicals for which inflammation persists for 14 days in at least 2 animals, is warranted (UN 2013). Moderate skin irritation was reported when undecylenic acid was applied to guinea pig skin under occlusive conditions. However, ToxServices considered this to be a conservative study because the OECD 404 Guideline recommends that exposure take place under semi-occlusive conditions (OECD 2002). In a continuous patch test in humans, exposure to concentrations up to 80% undecylenic acid was not irritating under non-occlusive conditions; irritation was reported when exposure occurred under occlusive conditions. Based on the OECD Guideline study in rabbits, ToxServices conservatively classified undecylenic acid as GHS Category 2, as reversibility of the mild irritant effects by day 14 could not be confirmed. This corresponds to a score of High, and is supported by the self-classification of H315 by all 1,079 notifiers to REACH. Confidence in the score is reduced because observations were not conducted at day 14.

**Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): H**

Undecylenic acid was assigned a score of High for eye irritation/corrosivity based on a GLP-compliant eye irritation study conducted according to OECD Guideline 405. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when the chemical is classified as GHS Category 2A (eye irritant) (CPA 2012b).

- **Authoritative and Screening Lists**
  - **Authoritative:** not on any authoritative lists
  - **Screening:** New Zealand HSNO/GHS: 6.4A – Irritating to the eye – GHS Category 2 (GHS-New Zealand does not differentiate between GHS Category 2A and 2B)
    - Classification is based on an R phrase (R36) listed on an MSDS (EPA 2015)
- **ECHA 2015b**
  - Undecylenic acid was irritating in a GLP-compliant eye irritation study conducted according to OECD Guideline 405 using male New Zealand White rabbits. Undiluted undecylenic acid (100 mg) was instilled into the eyes of four rabbits, and animals were observed for 15 days. Irritation was assessed at 1, 24, 48, and 72 hours and mean values for chemosis, redness of conjunctiva, iris lesions, and corneal opacity were calculated. Treatment caused chemosis (mean scores = 3/2/2.7) that persisted until day 15; conjunctival redness (mean score = 2/1.7/1.7) that persisted until day 10; iris lesions (mean score = 1/0.3/1) in 2 rabbits that persisted until day 11; and corneal opacity (mean score = 1.7/1/1) that persisted until day 13. The study authors concluded that undecylenic acid was irritating to the eye and should be classified as a Category 2 eye irritant.
- **Based on the weight of evidence, a score of High was assigned.** GHS guidance specifies that substances that produce in at least 2 of 3 tested animals a positive response of: (a) corneal opacity ≥ 1; and/or (b) iritis ≥ 1; and/or (c) conjunctival redness ≥ 2; and/or (d) conjunctival edema (chemosis) ≥ 2 calculated as the mean scores following grading at 24, 48, and 72 hours after instillation of the test material, and which fully reverse within an observation period of normally 21 days should be classified as GHS Category 2A (eye irritant) (UN 2013). As undecylenic acid produced scores ≥ 1 for corneal opacity and iritis, and ≥ 2 for chemosis in at least 2 of 3 animals, and irritation was fully reversible within 21 days, undecylenic acid was classified as GHS Category 2A and a score of High was assigned.
Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): vH
Undecylenic acid was assigned a score of Very High for acute aquatic toxicity based on EC₅₀ value of 0.24 mg/L in algae. GreenScreen® criteria classify chemicals as a Very High hazard for acute aquatic toxicity when acute aquatic toxicity values are less than 1 mg/L (CPA 2012b).
- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
  - Other: New Zealand HSNO/GHS – 9.1D (fish) – Slightly harmful in the aquatic environment or are otherwise designed for biocidal action
- ECHA 2015b
  - 72h LC₅₀ = 32.3 mg/L (*Oncorhynchus mykiss*, fish) (GLP, OECD 203)
  - 48h EC₅₀ = 28 mg/L (*Daphnia magna*, daphnia) (GLP, OECD 202)
  - 72h EC₅₀ = 0.24 mg/L (*Pseudokirchnerella subcapitata*, algae) (GLP, OECD 201)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): vH
Undecylenic acid was assigned a score of Very High for chronic aquatic toxicity based on the EC₁₀ value of 0.21 mg/L (no NOEC was identified) and estimated ChV of 0.06 mg/L for algae. GreenScreen® criteria classify chemicals as a Very High hazard for chronic aquatic toxicity when the chemical has a chronic aquatic toxicity value less than 0.1 mg/L (CPA 2012b). Confidence in the score is reduced because no experimental NOEC was reported.
- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
- ECHA 2015b
  - 21d NOEC = 2.9 mg/L (*Daphnia magna*, daphnia) (GLP, OECD 211)
  - 72h EC₁₀ = 0.21 mg/L (*Pseudokirchnerella subcapitata*, algae) (GLP, OECD 201)
- U.S. EPA 2012a
  - Undecylenic acid is designated to the Neutral Organics-ECOSAR chemical class. The most conservative predicted chronic values are 2.942 mg/L in fish, 2.695 mg/L in daphnia, and 10.440 mg/L in green algae. See Appendix F for modeling results.
- U.S. EPA 2013
  - Using the 74 hour EC₅₀ of 0.24 mg/L in algae (reported above) and the acute to chronic ratio of 4 for neutral organics, ToxServices calculated an estimated ChV of 0.06 mg/L⁹.
  - Based on the weight of evidence, a conservative score of Very High was assigned. As no measured values were identified for fish, modeling was performed. Modeling predicted a chronic aquatic toxicity value of 2.942 mg/L for fish. A measured NOEC of 2.9 mg/L was identified in daphnia. An EC₁₀ of 0.21 mg/L was identified in algae, but no NOEC was reported. Because the modeled ChV of 10.440 in algae is inconsistent with experimental data, ToxServices estimated a ChV of 0.06 using the acute to chronic ratio of 4 as recommended by U.S. EPA. ToxServices conservatively assigned a score of Very High based on the experimental EC₁₀ of 0.21 mg/L and estimated ChV of 0.06 mg/L in algae, as collectively these data indicate that chronic values for algae are likely to fall below the guidance value of 0.1 mg/L. GreenScreen® criteria specify a score of Very High when chemicals have chronic aquatic toxicity values less than 0.1 mg/L. Confidence in this score was reduced because no experimental NOEC was identified.

⁹ 0.24 mg/L ÷ 4 = 0.06 mg/L
Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL
Undecylenic acid was assigned a score of Very Low for persistence based on the findings of a GLP-compliant OECD 301 F test. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when the chemical primarily partitions to soil and it meets the 10-day window in a ready biodegradation test (CPA 2012b). Confidence in the score is reduced due to conflicting results between biodegradation studies.
- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists
- ECHA 2015b
  - Undecylenic acid was readily biodegradable in a GLP-compliant Manometric Respirometry Test conducted according to OECD Guideline 301 F. Undecylenic acid (initial concentration = 50 mg/L) achieved 74% degradation within 10 days and 94% degradation within 28 days. In the toxicity test, 70% degradation was found after 14 days; therefore, the test substance was not considered inhibitory to the inoculum. The study authors concluded that undecylenic acid was readily biodegradable and it met the 10-day window.
  - Undecylenic acid was not readily biodegradable in a GLP-compliant CO₂ Evolution Test conducted according to OECD Guideline 301 B. Undecylenic acid (initial concentration = 21 mg/L) achieved 38% degradation within 10 days and 51.5% degradation within 28 days. In the toxicity test, 81% degradation of the reference substance was found at the end of the test; therefore, the test substance was not considered inhibitory to the inoculum. The study authors concluded that undecylenic acid was not readily biodegradable.
- U.S. EPA 2012b
  - The BIOWIN modeling Ready Biodegradable Predictor indicates that undecylenic acid is expected to be readily biodegradable. Fugacity modeling predicts 72.7% will partition to soil with a half-life of 30 days, 26.5% will partition to water with a half-life of 15 days, and 0.515% will partition to air with a half-life of 5.29 hours. See Appendix G for modeling results.
- Based on the weight of evidence, a score of Very Low was assigned. Undecylenic acid was readily biodegradable and met the 10 day window in a GLP-compliant ready biodegradation test conducted according to OECD Guideline 301 F. Although it was not readily biodegradable in a test according to OECD Guideline 301 B, OECD guidance states that positive results in ready biodegradability tests can be considered valid despite negative results in other tests, provided the scientific quality and test conditions are adequate. (OECD 2001). Modeling also predicts that it is readily biodegradable. Fugacity modeling predicts that undecylenic acid will primarily partition to soil. GreenScreen® guidance specify a score of Very Low for chemicals that partition to soil and meet the 10-day window in a ready biodegradation test. Confidence in the score is reduced due to conflicting results between biodegradation studies.

Bioaccumulation (B) Score (vH, H, M, L, or vL): L
Undecylenic acid was assigned a score of Low for bioaccumulation based on modeling results. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when the BCF is
between 100 and 500 (CPA 2012b). Confidence in the score is reduced because it is based on modeled data.

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- ECHA 2015b
  - log $K_{ow} = 4$ (GLP, OECD 117)

- U.S. EPA 2012b
  - BCFBAF predicts a BCF of 347 based on a log $K_{ow}$ of 4 (measured). See Appendix G for modeling results.

- Based on the weight of evidence, a score of Low was assigned. No measured bioaccumulation data were located. Modeling predicted a bioconcentration factor (BCF) of 347 based on a measured log $K_{ow}$ of 4. GreenScreen® criteria specify a score of Low when the BCF is between 100 and 500. Confidence in the score is reduced because it is based on modeled data.

**Physical Hazards (Physical)**

**Reactivity (Rx) Score ($vH, H, M,$ or L): L**
Undecylenic acid was assigned a score of Low for reactivity based on the absence of explosive and self-reactive properties. Confidence in this score was reduced due to the absence of measured data. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when adequate data are available and the chemical is not GHS classified (CPA 2012b).

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- CHCS 2015
  - Undecylenic acid has no explosive or self-reactive properties (Bretherick and Urban 1999; UN 2009). See Appendix H for full list of explosive and self-reactive properties.

- Sigma-Aldrich 2014
  - Undecylenic acid has a physical hazard HMIS (Hazardous Materials Identification System) rating of 0. A physical hazard HMIS rating of 0 corresponds to “Materials that are normally stable, even under fire conditions, and will NOT react with water, polymerize, decompose, condense, or self-react. Non-Explosives.” (Paint.org 2015)

**Flammability (F) Score ($vH, H, M,$ or L): L**
Undecylenic acid was assigned a score of Low for flammability based on the findings of a flammability test. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate data are available and the chemical is not GHS classified (CPA 2012b).

- Authoritative and Screening Lists
  - Authoritative: not on any authoritative lists
  - Screening: not on any screening lists

- ECHA 2015b
  - Undecylenic acid was not flammable in a flammability test conducted according to EU Method A.10 (flammability solids). Authors of the study concluded that undecylenic acid is non-flammable.
References


European Chemicals Agency (ECHA). 2015b. REACH Dossier for Undec-10-enolic Acid (CAS# 112-38-9). Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-97d64c7a-7ba3-4ce7-e044-00144f67d031/DISS-97d64c7a-7ba3-4ce7-e044-00144f67d031_DISS-97d64c7a-7ba3-4ce7-e044-00144f67d031_DISS-97d64c7a-7ba3-4ce7-e044-00144f67d031.html.


Pharos. 2015. Pharos Chemical and Material Library Entry for Undecylenic Acid (CAS #112-38-9). Available at: http://www.pharosproject.net/material/


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 Undecylenic Acid (CAS #112-38-9)

## Table 1: Hazard Table

<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS#</th>
<th>Group I Human</th>
<th>Group II and II* Human</th>
<th>Ecotox</th>
<th>Fate</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Carcinogenicity</td>
<td>Mutagenicity/Genotoxicity</td>
<td>Reproductive Toxicity</td>
<td>Developmental Toxicity</td>
<td>Endocrine Activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>*</td>
</tr>
<tr>
<td>No</td>
<td>Undecylenic Acid</td>
<td>112-38-9</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
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## Table 2: Chemical Details

<table>
<thead>
<tr>
<th>Inorganic Chemical?</th>
<th>Chemical Name</th>
<th>CAS#</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Undecylenic Acid</td>
<td>112-38-9</td>
</tr>
</tbody>
</table>

## Table 3: Hazard Summary Table

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>2</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<td>No</td>
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<tr>
<td>3</td>
<td>STOP</td>
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<td>4</td>
<td>STOP</td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Table 4: Preliminary GreenScreen® Benchmark Score

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Preliminary GreenScreen® Benchmark Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undecylenic Acid</td>
<td>2</td>
</tr>
</tbody>
</table>

## Note:
- Chemical has not undergone a data gap assessment. Not a Final GreenScreen® Score.
- Data gap assessment: Not a Final GreenScreen® Score.

## Table 5: Data Gap Assessment Table

<table>
<thead>
<tr>
<th>Datagap Criteria</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
<th>h</th>
<th>i</th>
<th>j</th>
<th>End Result</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
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<td>Yes</td>
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<td>1</td>
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<tr>
<td>4</td>
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<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
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</tbody>
</table>

## Table 6: Final GreenScreen® Benchmark Score

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Final GreenScreen® Benchmark Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undecylenic Acid</td>
<td>2</td>
</tr>
</tbody>
</table>

Notes:
- Data gap assessment: Not a Final GreenScreen® Score.
- Preliminary GreenScreen® Benchmark Score is 1.
APPENDIX C: Pharos Output for Undecylenic Acid (CAS #112-38-9)

[112-38-9] 10-UNDECENOIC ACID

Direct Hazards:

- **MAMMALIAN**
  - New Zealand HSNO/GHS - 6.1A (dermal) - Acutely toxic
  - New Zealand HSNO/GHS - 6.1E (oral) - Acutely toxic

- **EYE IRRITATION**
  - New Zealand HSNO/GHS - 6.4A - Irritating to the eye

- **SKIN IRRITATION**
  - New Zealand HSNO/GHS - 6.3A - Irritating to the skin

- **ACUTE AQUATIC**
  - New Zealand HSNO/GHS - 9.1D (fish) - Slightly harmful in the aquatic environment or are otherwise designed for biocidal action

- **RESTRICTED LIST**
  - German FEA - Substances Hazardous to Waters (VwVwS) - Class 1 Low Hazard to Waters
  - Environment Canada - Domestic Substances List - Inherently Toxic to Humans: DSL substances that meet human health categorization criteria

Potential Residual Hazards:

See Life Cycle Research tab for details on residuals and other substances used in manufacture.

None identified
APPENDIX D: OECD Toolbox Carcinogenicity and Genotoxicity Modeling Results for Undecylenic Acid (CAS #112-38-9)
APPENDIX E: Toxtree Carcinogenicity Modeling Results for Undecylenic Acid (CAS #112-38-9)
APPENDIX F: ECOSAR Modeling Results for Undecylenic Acid (CAS #112-38-9)

ECOSAR Version 1.11 Results Page

SMILES: O=C(O)CCCCCCCCC=C
CHEM: 10-Undecenoic acid
CAS Num: 000112-38-9
ChemID1:
MOL FOR: C11 H20 O2
MOL WT: 184.28
Log \( K_{ow} \): 4.370 (EPISuite \( K_{ow} \)win v1.68 Estimate)
Log \( K_{ow} \): 4.000 (User Entered)
Log \( K_{ow} \): 3.86 (PhysProp DB exp value - for comparison only)
Melt Pt: 21.20 (deg C, User Entered for Wat Sol estimate)
Melt Pt: 24.50 (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 154.8 (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol: 38.46 (mg/L, User Entered)
Wat Sol: 73.7 (mg/L, PhysProp DB exp value)

--------------------------------------
Values used to Generate ECOSAR Profile
--------------------------------------
Log \( K_{ow} \): 4.000 (User Entered)
Wat Sol: 38.46 (mg/L, User Entered)

--------------------------------------
Available Measured Data from ECOSAR Training Set
--------------------------------------
No Data Available

--------------------------------------
ECOSAR v1.1 Class-specific Estimations
--------------------------------------

**************************************************************************
* ALERT: The chemical you are assessing has structural features  *
* associated with known surfactant classes. If the chemical has  *
* surfactant properties, the user may consider evaluation under:  *
*                                                                        *
* ----------------> Surfactants-Anionic  *
*                                                                        *
* Within the Special_Classes-Surfactants arm of ECOSAR (Menu Bar/Special *
* Classes  *
**************************************************************************
| Not Related to an Existing ECOSAR Class Definition |
| Estimates provided below use the Neutral Organics QSAR equations which |
| represent baseline toxicity potential (minimum toxicity) assuming a simple |
| non-polar narcosis model. Without empirical data on structurally similar |
| chemicals, it is uncertain if this substance will present significantly |
| higher toxicity above baseline estimates. |

Neutral Organics-acid:

<table>
<thead>
<tr>
<th>ECOSAR Class</th>
<th>Organism</th>
<th>Duration</th>
<th>End Pt</th>
<th>mg/L (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutral Organics-acid</td>
<td>Fish</td>
<td>96-hr.</td>
<td>LC50</td>
<td>24.204</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Daphnid</td>
<td>48-hr.</td>
<td>LC50</td>
<td>16.530</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Green Algae</td>
<td>96-hr.</td>
<td>EC50</td>
<td>26.423</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Fish</td>
<td>ChV</td>
<td></td>
<td>2.942</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Daphnid</td>
<td>ChV</td>
<td></td>
<td>2.695</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Green Algae</td>
<td>ChV</td>
<td></td>
<td>10.440</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Fish (SW)</td>
<td>96-hr.</td>
<td>LC50</td>
<td>30.838</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Mysid</td>
<td>96-hr.</td>
<td>LC50</td>
<td>5.913</td>
</tr>
<tr>
<td>Neutral Organics-acid</td>
<td>Fish (SW)</td>
<td>ChV</td>
<td></td>
<td>11.352</td>
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<tr>
<td>Neutral Organics-acid</td>
<td>Mysid (SW)</td>
<td>ChV</td>
<td></td>
<td>0.283</td>
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<tr>
<td>Neutral Organics-acid</td>
<td>Earthworm</td>
<td>14-day</td>
<td>LC50</td>
<td>1987.377 *</td>
</tr>
</tbody>
</table>

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

Class Specific LogK\textsubscript{ow} Cut-Offs

If the log K\textsubscript{ow} of the chemical is greater than the endpoint specific cut-offs presented below, then no effects at saturation are expected for those endpoints.

Neutral Organics:

Maximum LogK\textsubscript{ow}: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogK\textsubscript{ow}: 6.0 (Earthworm LC50)
Maximum LogK\textsubscript{ow}: 6.4 (Green Algae EC50)
Maximum LogK\textsubscript{ow}: 8.0 (ChV)
APPENDIX G: EPISuite Modeling Results for Undecylenic Acid (CAS #112-38-9)

CAS Number: (null)
SMILES: C(CCCCC=C)CCCC(=O)(O)
CHEM:
MOL FOR: C11 H20 O2
MOL WT: 184.28

EPI SUMMARY (v4.11)

Physical Property Inputs:
- Log $K_{ow}$ (octanol-water): 4.00
- Boiling Point (deg C): 286.00
- Melting Point (deg C): 21.20
- Vapor Pressure (mm Hg): 0.000144
- Water Solubility (mg/L): 38.46
- Henry LC (atm-m$^3$/mole): -----

Log Octanol-Water Partition Coef (SRC):
- Log $K_{ow}$ ($K_{ow}$WIN v1.68 estimate) = 4.37
- Log $K_{ow}$ (Exper. database match) = 3.86

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
- Boiling Pt (deg C): 293.11 (Adapted Stein & Brown method)
- Melting Pt (deg C): 71.46 (Mean or Weighted MP)
- VP (mm Hg, 25 deg C): 0.00409 (Modified Grain method)
- VP (Pa, 25 deg C): 0.545 (Modified Grain method)
- MP (exp database): 24.5 deg C
- BP (exp database): 275 deg C
- VP (exp database): 9.37E-04 mm Hg (1.25E-001 Pa) at 25 deg C

Water Solubility Estimate from Log $K_{ow}$ (WSK$ow$ v1.42):
- Water Solubility at 25 deg C (mg/L): 154.8
  log $K_{ow}$ used: 4.00 (user entered)
  melt pt used: 21.20 deg C
- Water Sol (Exper. database match) = 73.7 mg/L (30 deg C)

Water Sol Estimate from Fragments:
- Wat Sol (v1.01 est) = 35.962 mg/L

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

Henry's Law Constant (25 deg C) [HENRYWIN v3.20]:
- Bond Method: 5.23E-006 atm-m$^3$/mole (5.30E-001 Pa-m$^3$/mole)
- Group Method: 2.08E-006 atm-m$^3$/mole (2.11E-001 Pa-m$^3$/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
  HLC: 9.079E-007 atm-m³/mole (9.199E-002 Pa-m³/mole)
  VP: 0.000144 mm Hg (source: User-Entered)
  WS: 38.5 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KowWIN v1.10]:
  Log Kow used: 4.00 (user entered)
  Log Kaw used: -3.670 (HenryWin est)
    Log Ko(a) (KowWIN v1.10 estimate): 7.670
    Log Ko(a) (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
  Biowin1 (Linear Model): 0.7325
  Biowin2 (Non-Linear Model): 0.7379
Expert Survey Biodegradation Results:
  Biowin3 (Ultimate Survey Model): 3.1565 (weeks)
  Biowin4 (Primary Survey Model): 3.9674 (days)
MITI Biodegradation Probability:
  Biowin5 (MITI Linear Model): 0.7590
  Biowin6 (MITI Non-Linear Model): 0.8655
Anaerobic Biodegradation Probability:
  Biowin7 (Anaerobic Linear Model): 1.0102
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): 0.0192 Pa (0.000144 mm Hg)
  Log Ko(a) (Kowwin est): 7.670
  Kp (particle/gas partition coef. (m³/µg)):
    Mackay model: 0.000156
    Octanol/air (Koa) model: 1.15E-005
Fraction sorbed to airborne particulates (phi):
  Junge-Pankow model: 0.00561
  Mackay model: 0.0123
  Octanol/air (Koa) model: 0.000918

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
  Hydroxyl Radicals Reaction:
    OVERALL OH Rate Constant = 37.3087 E-12 cm³/molecule-sec
    Half-Life = 0.287 Days (12-hr day; 1.5E6 OH/cm³)
    Half-Life = 3.440 Hrs.
  Ozone Reaction:
    OVERALL Ozone Rate Constant = 1.200000 E-17 cm³/molecule-sec
    Half-Life = 0.955 Days (at 7E11 mol/cm³)
    Half-Life = 22.920 Hrs.
  Fraction sorbed to airborne particulates (phi):
0.00898 (Junge-Pankow, Mackay avg)
0.000918 (K_{ow} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):

K_{oc}: 175.2 L/kg (MCI method)
Log K_{oc}: 2.244 (MCI method)
K_{oc}: 233.5 L/kg (K_{ow} method)
Log K_{oc}: 2.368 (K_{ow} 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 = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 0.0901 days (HL = 1.231 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.540 (BCF = 347)
Log BAF Arnot-Gobas method (upper trophic) = 2.541 (BAF = 347.3)
log K_{ow} used: 4.00 (user entered)

Volatilization from Water:
Henry LC: 9.08E-007 atm-m/mole (calculated from VP/WS)
Half-Life from Model River: 876.8 hours (36.54 days)
Half-Life from Model Lake: 9679 hours (403.3 days)

Removal In Wastewater Treatment:
Total removal: 30.09 percent
Total biodegradation: 0.32 percent
Total sludge adsorption: 29.74 percent
Total to Air: 0.04 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:

<table>
<thead>
<tr>
<th>Mass Amount</th>
<th>Half-Life (hr.)</th>
<th>Emissions (kg/hr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0.515</td>
<td>5.29</td>
</tr>
<tr>
<td>Water</td>
<td>26.5</td>
<td>360</td>
</tr>
<tr>
<td>Soil</td>
<td>72.7</td>
<td>720</td>
</tr>
<tr>
<td>Sediment</td>
<td>0.229</td>
<td>3.24e+003</td>
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</table>

Persistence Time: 454 hr.
APPENDIX H: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List

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

CLP - Substances
### Explosivity – Full List

<table>
<thead>
<tr>
<th>Chemical group</th>
<th>Chemical Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>-C=CC-</td>
<td>Acetylenic Compounds</td>
</tr>
<tr>
<td>-C≡C-Metal</td>
<td>Metal Acetylides</td>
</tr>
<tr>
<td>-C≡C-Halogen</td>
<td>Haloacetylene Derivatives</td>
</tr>
<tr>
<td>(\text{CN}_2)</td>
<td>Diazo Compounds</td>
</tr>
<tr>
<td>-N=O -NO₂</td>
<td>Nitroso and Nitro Compounds</td>
</tr>
<tr>
<td>R-O-N=O</td>
<td>Acyl or Alkyl Nitrites and Nitrates</td>
</tr>
<tr>
<td>R-O-NO₂</td>
<td></td>
</tr>
<tr>
<td>(\text{C}≡\text{C}≡\text{O})</td>
<td>1,2-Epoxides</td>
</tr>
<tr>
<td>(\text{C}≡\text{N}≡\text{O}≡\text{Metal})</td>
<td>Metal Fulminates or aci-Nitro Salts</td>
</tr>
<tr>
<td>(\text{N}≡\text{Metal})</td>
<td>N-Metal Derivatives (especially heavy metals)</td>
</tr>
<tr>
<td>(\text{N}=\text{N}=\text{O}≡\text{N}=\text{NO}_2)</td>
<td>N-Nitroso and N-Nitro Compounds</td>
</tr>
<tr>
<td>(\text{N}≡\text{N}=\text{NO}_2)</td>
<td>N-Azolium Nitroimidates</td>
</tr>
<tr>
<td>(\text{C}≡\text{N}≡\text{N}≡\text{C})</td>
<td>Azo Compounds</td>
</tr>
<tr>
<td>Ar-N=N-O-Ar</td>
<td>Arene Diazoates</td>
</tr>
<tr>
<td>((\text{ArN=N})_2\text{O}, (\text{ArN=N})_2\text{S})</td>
<td>Bis-Arenediazo Oxides and Sulfides</td>
</tr>
<tr>
<td>RN=NR’R”&quot;</td>
<td>Triazaines</td>
</tr>
<tr>
<td>(\text{N}≡\text{N}≡\text{N})</td>
<td>High-nitrogen Compounds: e.g. Triazoles, Tetrazoles</td>
</tr>
<tr>
<td>Chemical group</td>
<td>Chemical Class</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>[1] ROOR',</td>
<td>Peroxy Compounds:</td>
</tr>
<tr>
<td></td>
<td>[1] Alkyl hydroperoxides (R'_H), Peroxides (R'=organic):</td>
</tr>
<tr>
<td></td>
<td>[2] Peroxo acids (R'_H), Peroxyesters (R'=organic)</td>
</tr>
<tr>
<td>[2] ( \text{-C^\circ^{\text{\text{o}}}\text{-O}} )</td>
<td>Metal peroxides, Peroxoacids salts</td>
</tr>
<tr>
<td>[2] ( \text{-C^\circ^{\text{\text{o}}}\text{-O}^-} \text{Metal}^+ )</td>
<td>Azides e.g. ( \text{PbN}_6, \text{CH}_3\text{N}_3 )</td>
</tr>
<tr>
<td>( \text{O}^-\text{-C-N}_2^+ )</td>
<td>Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide</td>
</tr>
<tr>
<td>( \text{Ar-N=N-S-} )</td>
<td>Diazonium sulfides and derivatives, Arenediazo Aryl Sulfides</td>
</tr>
<tr>
<td>( \text{Ar-N=N-S-Ar} )</td>
<td></td>
</tr>
<tr>
<td>( \text{XO}_2 )</td>
<td>Halogen Oxide: e.g. perchlorates, bromates, etc</td>
</tr>
<tr>
<td>( \text{NX}<em>3, \text{e.g. NC}</em>{12}, \text{RNC}_{12} )</td>
<td>N-Halogen Compounds</td>
</tr>
</tbody>
</table>

Adapted from Bretherick (Bretherick’s Handbook of Reactive Chemical Hazards 6th Ed., 1999, Butterworths. London)
Self-Reactive Substances

**Screening procedures**

- Not in CLP, but UN Manual of Tests and Criteria Appendix 6
- No explosive groups (see 2.1) plus

<table>
<thead>
<tr>
<th>Structural feature</th>
<th>Chemical classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutually reactive groups</td>
<td>Aminonitriles, haloanilines, organic salts of oxidising agents</td>
</tr>
<tr>
<td>S=O</td>
<td>Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides</td>
</tr>
<tr>
<td>P=O</td>
<td>Phosphites</td>
</tr>
<tr>
<td>Strained rings</td>
<td>Epoxides, aziridines</td>
</tr>
<tr>
<td>Unsaturation</td>
<td>Olefins, cyanates</td>
</tr>
</tbody>
</table>

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CLP - Substances

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Licensed GreenScreen® Profilers

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