ISODODECANE

(CAS #31807-55-3)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: February 25, 2025[1]

Expiration Date: February 25, 2030

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[1] The report was last updated on February 25, 2025. However, the last complete literature search was conducted on December 27, 2024.

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GreenScreen® Executive Summary for Isododecane (CAS #31807-55-3)

Isododecane is a branched aliphatic hydrocarbon (i.e., isoparaffin) isolated from petroleum. It is a colorless liquid that is insoluble in water and flammable. The boiling point of less than 250°C and the vapor pressure of > 0.075 mmHg indicate that it is a volatile organic compound (VOC). Isododecane is used as a solvent, perfuming agent, and emollient in cosmetics. It is also used as a dispensing agent for high-reactivity organic peroxide catalysts in polymerization reactions. Isododecane is part of a mixture serving as an alternative ingredient for volatile silicone emollients in personal care products. Silicone residuals such as octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) are of concern due to the persistent, bioaccumulative, and toxic (PBT) properties, and are banned for use in personal care products at concentrations > 0.1% under the REACH regulation in the European Union (EU).

Isododecane has been evaluated by the U.S. Cosmetic Ingredient Review (CIR) Expert Committee as a member of the isoparaffins group. It has not been evaluated by the European Scientific Committee on Consumer Safety (SCCS), nor is it listed on Annex II or III of the EC Cosmetics Regulation. Isododecane is listed on the Chinese Food and Drug Administration's Cosmetics Ingredients List, but not on California's Safe Cosmetics Program's Reportable Ingredients List or Canada's Cosmetic Ingredient Hotlist.

Isododecane 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 2d
    - High bioaccumulation-B + Very High Ecotoxicity (chronic aquatic-CA)
    - High bioaccumulation-B + Moderate Group II Human (neurotoxicity single exposure-Ns)
    - High bioaccumulation-B + High Group II Human (systemic toxicity-single exposure -STs and skin irritation-IrS)
- Benchmark 2f
    - Very High Ecotoxicity (chronic aquatic-CA)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), isododecane meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if isododecane were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in vitro* testing for mutagenicity and *in silico* modeling for carcinogenicity, respiratory sensitization, chronic aquatic toxicity, persistence, and bioaccumulation. The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties:

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

Type I (input data) uncertainties in isododecane's NAMs dataset include lack of, or insufficient experimental data for carcinogenicity and respiratory sensitization, and lack of validated test methods for respiratory sensitization. Isododecane's Type II (extrapolation output) uncertainties include the lack of defined applicability domains of some modeling programs, limitations of *in vitro* genotoxicity assays in assessing only a few processes in genotoxicity and not completely mimicking *in vivo* metabolism, and respiratory sensitization alerts' lack of consideration of non-immunological mechanisms.

GreenScreen® Hazard Summary for Isododecane

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
						s	r*	s	r*	*	*								
L	**L**	**L**	**L**	DG	**L**	*H*	**L**	*M*	*L*	**L**	*L*	**H**	**L**	*L*	*vH*	*L*	*H*	*L*	**M**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that 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. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Chemical Assessment for Isododecane (CAS #31807-55-3)

Method Version: GreenScreen® Version 1.4
Assessment Type[2]: Certified
Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment (v.1.4) Prepared By:
Name: John Lee, M.P.H.
Title: Toxicologist
Organization: ToxServices LLC
Date: December 23, 2024; February 19, 2025

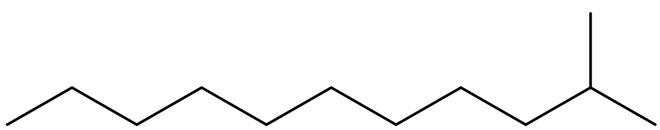
Quality Control Performed By:
Name: Jennifer Rutkiewicz, Ph.D.
Title: Senior Chief Toxicologist
Organization: ToxServices LLC
Date: December 27, 2024; February 25, 2025

Expiration Date: February 25, 2030[3]

Chemical Name: Isododecane

CAS Number: 31807-55-3

Chemical Structure(s):



Isododecane (CAS #31807-55-3)

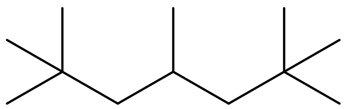
Also called:
2-Methylundecane; Undecane, 2-methyl-; 2,2,4,6,6-Pentamethylheptane; 2-Methylhendecane; Isododecane; 2-Methyl undecane (PubChem 2024).

There are two discrete structures associated with the INCI name isododecane – the IUPAC name 2-methylundecane (CAS #31807-55-3) the IUPAC name 2,2,4,6,6-pentamethylheptane (CAS #13475-82-693685-81-5), and the INCI name isododecane is also associated with the CAS #13475-82-6, which appears to correspond to a mixture of isomers (PubChem 2024). This review will focus on the 2-methylundecane structure associated with CAS #31807-55-3.

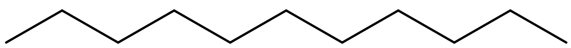
Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
Limited data are available for isododecane (CAS #31807-55-3) from the OECD SIDS initial assessment profile on the C9-14 aliphatic (≤2% aromatic) hydrocarbon solvent category (OECD 2012a) and the CIR assessment on isoparaffins (CIR 2012). CIR identifies 2,2,4,6,6-pentamethylheptane (CAS #13475-82-6) as falling under the INCI name isododecane, and the REACH registration dossier (ECHA CHEM 2024) for this chemical contains read-across to additional structurally similar hydrocarbons. These read-across surrogates in the REACH registration dossier are also included in the previously mentioned OECD SIDS initial assessment profile on C9-14 aliphatic (≤2% aromatic) hydrocarbon solvent category and the CIR on isoparaffins. The surrogates used in this assessment, most of which are mixtures and

[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent).
[3] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment expires three years from the date of completion if completed before January 1, 2019 (CPA 2018a).

therefore do not have a single representative structure, are listed below. It should be noted that ToxServices included data only on chemicals or mixtures for which composition was clearly identified by the secondary sources; therefore, some studies reported in the ECHA, OECD, and CIR sources are not included in this assessment. In addition, because aromatic hydrocarbons generally have a higher order of toxicity than aliphatic hydrocarbons, mixtures containing high percentages of aromatic compounds are considered to be conservative surrogates, and are included only when no data or insufficient data are available for the stronger surrogates.

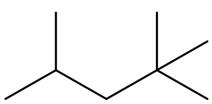


2,2,4,6,6-Pentamethylheptane (CAS #13475-82-6)



Undecane (CAS #1120-21-4)

Decane (CAS #124-18-5)



Isooctane (CAS #540-84-1)

Additional Surrogates:
C10-14 normal paraffins (CAS #N/A)
C13 normal paraffins (CAS #N/A)
C10-12 normal paraffins (CAS #N/A)
C12-14 normal paraffins (CAS #N/A)
C11 and C12 normal paraffins (CAS #N/A)
Stoddard solvent IIC, (saturated aliphatic and alicyclic C7-C12 hydrocarbons with boiling points 130°C-220°C) (CAS #64742-88-7)
Naphtha (petroleum), heavy alkylate (predominantly branched saturated C9-C12 hydrocarbons with boiling points 150°C-220°C) (CAS #64741-65-7)
Hydrocarbons, C9-11, n-alkanes, isoalkanes, cyclics, <2% aromatics (CAS #64742-48-9)
Hydrocarbons, C10-12 isoalkanes, with <2% aromatics (CAS #N/A)
Hydrocarbons, C11-12 isoalkanes, with <2% aromatics (CAS #N/A)
Hydrocarbons, C11-13 isoalkanes, with <2% aromatics (CAS #N/A)
Hydrocarbons, C12-16 isoalkanes, with <2% aromatics (CAS #N/A)
Hydrocarbons, C12-16 n-alkanes, isoalkanes and cyclics, <2% aromatics (CAS #N/A)
Hydrocarbons, C10-12 isoalkanes and cyclics, <2% aromatics (CAS #N/A)
Hydrocarbons, C10-14 isoalkanes and cyclics, <2% aromatics (CAS #N/A)
Hydrocarbons, C12-13 isoalkanes and cyclics, <2% aromatics (CAS #N/A)
C10-13 isoparaffins/isoalkanes (CAS #N/A)
Paraffins (petroleum), normal C5-20 (CAS #64771-72-8)

Distillates (petroleum), hydrotreated light (predominantly C11-C14 paraffins and naphthenes) (CAS #64742-47-8)
Jet fuel JP-8 (C9-C16 aliphatic carbons, <25% aromatics) (CAS #N/A)
Hydrodesulfurized kerosene (C9-C16 petroleum fuel containing approximately 80% aliphatic and 20% aromatic (primarily alkylated single ring compounds)) (CAS #64742-82-1)
C9-12 isoalkanes (CAS #90622-57-4)
C10-14 paraffins (CAS #93924-07-3)
White spirits (C9-11 aliphatic hydrocarbon solvent with 15-20% aromatics) (CAS #N/A)
Light alkylate naphtha distillate (mainly C5-C8 isoparaffins) (CAS #64741-66-8)
C11-13 isoparaffin (CAS #N/A)
C12-15 isoparaffin (CAS #N/A)

Identify Applications/Functional Uses: (EC 2024)
1. Solvent
2. Emollient
3. Perfuming

Known Impurities[4]:
Common impurities include C_6 and C_{16} hydrocarbons (2% max), aromatics (1 mg/kg max), carbonyls (5 mg/kg max), sulfur (1 mg/kg max), peroxides (1 mg/kg max as hydrogen peroxide), and water (50 mg/kg max) (CIR 2012). The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Isododecane[5,6 7,8]: Isododecane was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score combinations:
- Benchmark 2d
  - High bioaccumulation-B + Very High Ecotoxicity (chronic aquatic-CA)
  - High bioaccumulation-B + Moderate Group II Human (neurotoxicity single exposure-Ns)
  - High bioaccumulation-B + High Group II Human (systemic toxicity-single exposure -STs and skin irritation-IrS)
- Benchmark 2f
  - Very High Ecotoxicity (chronic aquatic-CA)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), isododecane meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if isododecane were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

[4] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[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 v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[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 v1.4 Annex 2.

Figure 1: GreenScreen® Hazard Summary for Isododecane

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**
						s	r*	s	r*	*	*								
L	**L**	**L**	**L**	DG	**L**	*H*	**L**	*M*	*L*	**L**	*L*	*H*	**L**	**L**	*vH*	*L*	*H*	*L*	**M**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that 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. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

Environmental Transformation Products

C9-C14 aliphatic hydrocarbon solvents do not undergo hydrolysis as they do not contain hydrolysable functional groups. These compounds are also poorly susceptible to photolysis (OECD 2012a). No biodegradation products were identified.

Table 1: Environmental Transformation Product Summary

Life Cycle Stage	Transformation Pathway	Environmental Transformation Product	CAS #	Feasible (Yes or No)	Relevant (Yes or No)	GreenScreen® List Translator Score or GreenScreen® Benchmark™ Score[9,10]
N/A	N/A	None identified	N/A	N/A	N/A	N/A

Introduction

Isododecane is a branched aliphatic hydrocarbon (i.e., isoparaffin) isolated from petroleum. It is used as a solvent, perfuming agent, and emollient in cosmetics (EC 2024). It is also used as a dispensing agent for high-reactivity organic peroxide catalysts in polymerization reactions (Santa Cruz Biotechnology 2024, CIR 2012). Isododecane is part of a mixture serving as an alternative ingredient for volatile silicone emollients in personal care products (Cosmetics Business 2012). Silicone residuals such as octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) are of concern due to the persistent, bioaccumulative, and toxic (PBT) properties, and are banned for use in personal care products at concentrations > 0.1% under the REACH regulation in the European Union (EU) (ECHA 2019).

ToxServices assessed isododecane against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2021).

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

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2024a). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been

[9] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against the lists in the List Translator electronically.

[10] A GreenScreen® assessment of a transformation product depends on the Benchmark score of the parent chemical (see GreenScreen® Guidance).

assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2024b).

Isododecane is not listed on SCIL.

<u>GreenScreen® List Translator Screening Results</u>

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[11] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for isododecane can be found in Appendix C.

- Isododecane is an LT-UNK chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Isododecane is listed on the U.S. DOT list as a Hazard Class 3 chemical, Packing Group III.
- Isododecane is on the following list for multiple endpoints. Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.
    - German FEA - Substances Hazardous to Waters, Class 1 - Low Hazard to Waters

<u>Hazard Statement and Occupational Control</u>

Three Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements (EU, non-harmonized) were identified for isododecane, as indicated in Table 2. General personal protective equipment (PPE) recommendations are presented in Table 3, below. No occupational exposure limits (OELs) were identified.

Table 2: GHS H Statements for Isododecane (CAS #31807-55-3) (ECHA C&L 2024)	
H Statement	**H Statement Details**
H226	Flammable liquid and vapor
H304	May be fatal if swallowed and enters airways
H413	May cause long lasting harmful effects to aquatic life

Table 3: Occupational Exposure Limits and Recommended Personal Protective Equipment for Isododecane (CAS #31807-55-3)			
Personal Protective Equipment (PPE)	**Reference**	**Occupational Exposure Limits (OEL)**	**Reference**
Safety glasses, nitrile rubber gloves, and filter type ABEK	Millipore Sigma 2024	None	N/A

<u>Physicochemical Properties of Isododecane</u>

Isododecane is a colorless liquid that is insoluble in water and flammable. The boiling point of less than 180°C and the vapor pressure of higher than 0.735 mmHg indicate that it is a VOC. Insolubility in water and a log K_{ow} of 6.16 indicate that it is lipophilic.

[11] DOT lists are not required lists for GreenScreen® List Translator v1.4. They are reference lists only.

Table 4: Physical and Chemical Properties of Isododecane (CAS #31807-55-3)		
Property	**Value**	**Reference**
Molecular formula	$C_{12}H_{26}$	PubChem 2024
SMILES Notation	CCCCCCCCCC(C)C	PubChem 2024
Molecular weight	170.33 g/mol	PubChem 2024
Physical state	Liquid	Millipore Sigma 2024
Appearance	Colorless liquid	Millipore Sigma 2024
Melting point	≤ -50℃	ChemSrc 2024
Boiling point	177.1℃ 180℃	ChemSrc 2024 Millipore Sigma 2024
Vapor pressure	0.735 mmHg (temperature unspecified) 42 mmHg at 65°C 1.45 mmHg at 25°C (est.)	CIR 2012 Millipore Sigma 2024 U.S. EPA 2017
Water solubility	Insoluble	Millipore Sigma 2024
Dissociation constant	Not identified	N/A
Density/specific gravity	0.75 g/cm^3	ChemSrc 2024
Partition coefficient	Log P_{ow} = 6.338 Log K_{ow} = 6.16 (est.)	Millipore Sigma 2024 U.S. EPA 2017

Toxicokinetics

Isododecane is expected to exhibit similar toxicokinetics as the category members evaluated in the OECD SIDS initial assessment profile on C_9-C_{14} aliphatic (≤2% aromatic) hydrocarbon solvent category report (2012).

- OECD 2012a
  - *Absorption:* White spirit constituents are readily absorbed when inhaled. Materials in this category are readily absorbed through the lungs. An estimated 61% - 81% of a C_9-C_{14} hydrocarbon solvent would be absorbed when ingested. Dermal absorption is expected to be 0.01%/hr to 0.1%/hr.
  - *Distribution:* Members of the C_9-C_{14} aliphatic (2-25% aromatic) hydrocarbon solvents category are widely distributed throughout the body of both humans and animals and accumulate in the adipose tissues due to their lipophilic nature.
  - *Metabolism:* Aliphatic hydrocarbons undergo oxidative conversion, catalyzed by monooxygenases, to alcohols.
  - *Excretion:* It is expected that components or metabolites of complex hydrocarbon solvents such as Stoddard solvent/white spirit would be rapidly exhaled from the lungs.

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Isododecane was assigned a score of Low for carcinogenicity based on weight of evidence from rule-based (VEGA and Toxtree) and statistical-based (Danish QSAR) modeling programs. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). 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 2012a
  - *Inhalation:* *<u>Surrogate: Stoddard solvent IIC (CAS #64742-88-7):</u>* In a combined chronic toxicity / carcinogenicity study directed by National Toxicology Program (NTP), male and female F344 rats (50/sex/dose) were exposed to the Stoddard solvent IIC vapor via inhalation at levels of 0, 0.138 (males only), 0.55, 1.1, or 2.2 (females only) mg/L for 6 hour/day, 5 days/week for 105 weeks. In males, there was an increase in adrenal medulla neoplasms (benign pheochromocytoma). No treatment-related neoplasms were seen in females. NTP concluded that there was some evidence of carcinogenicity in male rats and no evidence of carcinogenicity in female rats.
  - *Inhalation:* *<u>Surrogate: Stoddard solvent IIC (CAS #64742-88-7):</u>* In a combined chronic toxicity / carcinogenicity study directed by NTP, male and female C6C3F1 mice (50/sex/dose) were exposed to the Stoddard solvent IIC vapor via inhalation at levels of 0, 0.55, 1.1, or 2.2 mg/L for 105 weeks. There was no evidence of carcinogenicity in males. In females there was an increase in liver tumors which was considered by NTP to be equivocal evidence of carcinogenicity because the tumors were secondary to an increase in body weight.
- Toxtree 2018
  - Isododecane does not contain a structural alert for genotoxic or nongenotoxic carcinogenicity (Appendix D).
- VEGA 2024
  - Isododecane was assessed for carcinogenicity with six models in the VEGA platform. If an external compound is beyond the defined scope of a given model, it is considered outside that model's applicability domain (AD) and cannot be associated with a reliable prediction (Sahigara 2007). Values for AD index (ADI) range from 0 (worst case) to 1 (best case). Generally, ADI values of > 0.70 indicate that the prediction has moderate or better predictivity (Gad 2016). Predictions with ADI > 0.7 and the corresponding ADI values are described below; the remaining models had ADI values < 0.7 and are not included:
    - IRFMN/ISSCAN-CGX v1.0.2 model predicts isododecane to be a possible non-carcinogen with moderate confidence. The ADI is 0.753, indicating that the prediction is reliable (Appendix E).
    - IRFMN oral classification v1.0.1 model predicts isododecane to be a non-carcinogen with high confidence. The ADI is 0.976, indicating that the prediction is reliable (Appendix E).
    - IRFMN inhalation classification v1.0.1 model predicts isododecane is a non-carcinogen with high confidence. The ADI is 0.976, indicating that the prediction is reliable (Appendix E).
- DTU 2024
  - Danish (Q)SAR Database for the CAS number 31807-55-3 reports that isododecane is in the domains of the E Ultra FDA RCA cancer models for the male rat (negative), female rat (negative), rat (negative), male mouse (negative), female mouse (negative), mouse (negative), and rodent (negative). Isododecane is out of the domains of all of the Leadscope FDA RCA cancer models. Regarding the liver specific cancer in rat or mouse model, it is in domain and negative of the Case Ultra model; isododecane is outside the applicability domain of the Leadscope model, the SciQSAR model, and the overall model battery (Appendix F).
- Based on a weight of evidence, a score of Low was assigned. Isododecane does not contain structural alerts for genotoxic or non-genotoxic carcinogenicity according to Toxtree. Three of the

six models in VEGA produced reliable predictions for carcinogenicity for isododecane, and it was predicted to be a non-carcinogen in all three models. All eight of the in domain results from the Danish QSAR modeling database gave negative predictions for carcinogenicity. The weight of evidence from rule-based (VEGA and Toxtree) and statistical-based (Danish QSAR) modeling programs indicates that isododecane is not likely to be carcinogenic. Furthermore, the equivocal results from the animal studies are not sufficient evidence of carcinogenicity. As Stoddard solvent IIC is a mixture, it is unknown which constituent(s) is/are responsible for the carcinogenic activity.

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

Isododecane was assigned a score of Low for mutagenicity/genotoxicity based on negative results from surrogates for gene mutation in bacteria and in mammalian cells *in vitro*, and for clastogenicity *in vitro* and *in vivo.* GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on experimental data from studies on the target chemical and a large number of 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.
- CIR 2012
    - *In vitro:* Isododecane was negative in a bacterial mutagenicity assay in *S. typhimurium* strains TA98 and TA100 at concentrations of 156 to 5,000 µg/plate. No additional details were provided.
    - *In vitro: <u>Surrogate: C11-13 isoparaffin (CAS #N/A):</u>* C11-13 isoparaffin was not mutagenic in an Ames reverse mutation assay in *S. typhimurium* strains TA98, TA100, TA1535, TA537, and TA1538 with and without metabolic activation. No additional information was provided.
    - *In vitro: <u>Surrogate: C11-13 isoparaffin (CAS #N/A):</u>* C10-13 isoparaffin was not mutagenic in an Ames reverse mutation assay in *S. typhimurium* strains TA98, TA100, TA1535, TA537, and TA1538 when tested at concentrations up to 10,000 µg/plate with and without metabolic activation. No additional information was provided.
    - *In vitro: <u>Surrogate: C11-13 isoparaffin (CAS #N/A):</u>* C10-13 isoparaffin was not mutagenic in an *in vitro* mammalian cell forward mutation assay conducted in L5178Y lymphoma cells when tested at concentrations up to 1,000 µg/mL with and without metabolic activation. No additional information was provided.
    - *In vitro: <u>Surrogate: C11-13 isoparaffin (CAS #N/A):</u>* C10-13 isoparaffin was negative in an *in vitro* sister chromatid exchange assay conducted in Chinese hamster ovary (CHO) cells when tested at concentrations up to those that caused cytotoxicity with and without metabolic activation. No additional information was provided
- ECHA CHEM, CAS #13475-82-6, 2024
    - *In vitro: <u>Surrogate: Naphtha (petroleum), heavy alkylate (CAS #64741-65-7):</u>* Naphtha (petroleum), heavy alkylate (tradename ShellSol TD) was negative in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 in *S. typhimurium* strains TA98, TA100, TA102, TA1535, and TA1537 at concentrations up to 5,000 µg/plate with and without metabolic activation (Klimisch 1, reliable without restriction).
    - *In vitro: <u>Surrogate: Hydrocarbons, C9-11, n-alkanes, isoalkanes, cyclics, <2% aromatics (CAS #64742-48-9):</u>* Hydrocarbons, C9-11, n-alkanes, isoalkanes, cyclics, <2% aromatics (tradename ShellSol D60) was negative in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 in *S. typhimurium* strains TA98, TA100,

TA102, TA1535, and TA1537 at concentrations up to 5,000 µg/plate with and without metabolic activation (Klimisch 1, reliable without restriction).
    - *In vitro: Surrogate: Paraffins (petroleum), normal C5-20 (CAS #64771-72-8):* Paraffins (petroleum), normal C5-20 (tradename Petrepar 120) was negative in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 in *S. typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 at concentrations up to 5,000 µg/plate with and without metabolic activation (Klimisch 2, reliable with restrictions).
    - *In vitro: Surrogate: C10-13 isoalkane (CAS #N/A):* C10-13 isoalkane was not mutagenic in a non-GLP *in vitro* mammalian cell forward mutation assay conducted in L5178Y lymphoma cells when tested at concentrations up to 1,000 µg/mL with and without metabolic activation. No additional information was provided (Klimisch 2, reliable with restrictions).
    - *In vitro: Surrogate: Distillates (petroleum), hydrotreated light (CAS #N/A):* Distillates (petroleum), hydrotreated light (tradename Shellsol D70) was negative in a GLP-compliant *in vitro* chromosomal aberration test similar to OECD Guideline 473 conducted in primary human lymphocytes at concentrations up to 1,000 µg/mL with and without metabolic activation. An increased incidence (statistically significant) of structural aberration was found at the lowest dose of 22.52 µg/mL in the absence of metabolic activation, but study authors considered this finding incidental as two repeat experiments did not find increased structural aberration at similar concentrations (Klimisch 1, reliable without restriction).
    - *In vivo: Surrogate: Distillates (petroleum), hydrotreated light (predominantly C11-C14 paraffins and naphthenes) (CAS #64742-47-8):* Distillates (petroleum), hydrotreated light (predominantly C11-C14 paraffins and naphthenes) (tradename MRD-89-582) was negative in a GLP-compliant *in vivo* micronucleus assay similar to OECD Guideline 474. CD-1 mice were exposed to a single gavage dose of 0, 1.25, 2.5, or 5.0 g/kg and sacrificed 24, 48, or 72 hours afterwards and bone marrow was collected. There were no clinical signs of toxicity or mortality in treated animals (Klimisch 1, reliable without restriction).

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

Isododecane was assigned a score of Low for reproductive toxicity based on a lack of reproductive effects observed in oral, dermal, and inhalation studies with multiple surrogates. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on experimental data from studies on multiple surrogates across all routes of exposure.

- 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 2012a
    - *Oral: Surrogate: Undecane (CAS #1120-21-4):* Undecane was tested in a GLP-compliant combined reproduction and developmental toxicity screening test similar to OECD Guideline 422. Sprague-Dawley rats (12/sex/dose) received undecane at doses of 0, 100, 300, or 1,000 mg/kg/day via gavage for 14 days prior to mating, through the mating period, and for a total of 46 days (males) or through lactation day 3 (females). There were no effects on the sex cycle of females, copulation and conception, pathological changes to the testis, epididymis, ovary, or number of pups. Additionally, there were no treatment related effects on the offspring survival, mean litter size, sex ratio, body weight, and external and internal abnormalities. Authors identified a NOAEL of 1,000 mg/kg/day, which was the highest dose tested.

- *Oral:* *<u>Surrogate: Jet fuel JP-8 (CAS #N/A):</u>* In a one-generation toxicity study similar to OECD Guideline 415, male Sprague-Dawley rats received jet fuel JP-8 by gavage at 0, 750, 1,500, or 3,000 mg/kg/day for 70 days and then mated with naïve females. Exposure continued for a total of 90 days. Males at the highest dose had significantly reduced body weight gain. However, there were no treatment-related effects on fertility, changes in sperm parameters, or histological effects on reproductive organs. Study authors identified a reproductive NOAEL of 3,000 mg/kg/day for male rats.
- *Oral:* *<u>Surrogate: Jet fuel JP-8 (CAS #N/A):</u>* In a one-generation toxicity study similar to OECD Guideline 415, female Sprague-Dawley rats received JP 8 by gavage at 0, 325, 750, or 1,500 mg/kg daily for 90 days and then mated with naïve males. Exposure continued for 21 weeks in total and included the gestation and lactation periods. The study was terminated on postnatal day 21. High dose females had significantly reduced weight gain. However, no treatment-related effects were found on fertility, gestation length, litter size, or live birth index. Offspring had reduced body weight gain, but the difference between groups reduced over time without treatment. Study authors identified a NOAEL of 1,500 mg/kg/day for female fertility and a NOAEL of 750 mg/kg/day for offspring based on reduced body weight correlating with decreased maternal body weight.
- *Dermal:* *<u>Surrogate: Hydrodesulfurized kerosene (CAS #64742-82-1):</u>* In a reproduction / developmental toxicity screening study conducted according to OECD Guideline 421, hydrodesulfurized kerosene was administered dermally to male and female Sprague-Dawley rats (10/sex) at doses of 0, 165, 330, or 494 mg/kg/day. Animals were treated 14 days prior to mating and through 2 weeks of mating and 20 days of gestation. There were no effects on mating, litter size, offspring body weights, or offspring survival. Authors identified a NOAEL of 494 mg/kg/day for reproductive toxicity. No additional details were provided.

- ECHA CHEM, CAS #13475-82-6, 2024
  - *Inhalation:* *<u>Surrogate: Stoddard solvent IIC (CAS #64742-88-7):</u>* In a GLP-compliant reproductive/developmental toxicity screening test similar to OECD Guideline 421, Sprague-Dawley rats (10 males and 40 females/dose) received whole body inhalation exposures to the vapor of a mixture of aromatic, paraffinic and naphthenic hydrocarbons with the tradename VARSOL 40 and sample name MRD-78-25 at 0, 100, or 300 ppm 6 hours per day, 5 days per week for 8 weeks. The supplier indicates that the mixture is similar to CAS # 64742-88-7 (Stoddard solvent) (Exxon Company 1979). After the exposure period, each male mated for one week each with two females, and the females were terminated 18 days after the beginning of mating. Examinations included mortality, clinical observations, body weight, gross necropsy, histopathology, number of implantation sites, early resorption sites, late resorption sites, and viable fetal swellings. There were no treatment-related effects on any of the parameters examined. Study authors identified a NOAEC of 300 ppm (equivalent to 1.72 mg/L according to ECHA dossier authors) for reproductive toxicity for this study (Klimisch 1, reliable without restriction).

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

Isododecane was assigned a score of Low for developmental toxicity based on a lack of toxicologically relevant effects noted in oral, dermal, and inhalation studies with surrogates. Although some oral studies reported effects on offspring body weights, the effects occurred only at very high oral doses which also resulted in effects on parental body weights and exceeded the suggested limit dose of 1,000 mg/kg/day for reproductive and developmental toxicity, and are thus likely related to maternal toxicity. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on experimental data from studies on multiple surrogates across all routes of exposure.

- 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 2012a
  - *Oral:* *<u>Surrogate: Undecane (CAS #1120-21-4):</u>* In the previously described GLP-compliant combined reproduction and developmental toxicity screening test similar to OECD Guideline 422, Sprague-Dawley rats (12/sex/dose) were administered undecane (purity 99%) at doses of 0, 100, 300, or 1,000 mg/kg/day via gavage for 14 days prior to mating, through the mating period, and for a total of 46 days (males) or through lactation day 3 (females). There were no treatment related effects on the offspring survival, mean litter size, sex ratio, body weight, and external and internal abnormalities. Authors identified a NOAEL of 1,000 mg/kg/day, which was the highest dose tested.
  - *Oral:* *<u>Surrogate: Jet fuel JP-8 (CAS #N/A):</u>* In the previously described one-generation toxicity study similar to OECD Guideline 415, female Sprague-Dawley rats received JP 8 by gavage at 0, 325, 750, or 1,500 mg/kg daily for 90 days and then mated with naïve males. Exposure continued for 21 weeks in total and included the gestation and lactation periods. The study was terminated on postnatal day 21. High dose females had significantly reduced weight gain. However, no treatment-related effects were found on fertility, gestation length, litter size, or live birth index. Offspring had reduced body weight gain, but the difference between groups reduced over time without treatment. Study authors identified a NOAEL of 1,500 mg/kg/day for female fertility and a NOAEL of 750 mg/kg/day for offspring based on reduced body weight correlating with decreased maternal body weight.
  - *Oral:* *<u>Surrogate: Jet fuel JP-8 (CAS #N/A):</u>* In a prenatal developmental toxicity study in Sprague-Dawley rats, pregnant animals received JP-8 by gavage on gestational days 6-15 at 0, 500, 1,000, 1,500, or 2,000 mg/kg/day. Increased mortality was found at the highest dose in maternal animals, but surviving dams had pregnancy rates, litter sizes and frequency of live fetuses/litter comparable to controls. Maternal weights were adversely affected in all treated groups, and fetal weights of the two highest dose groups were significantly reduced. There were no malformations upon uterine examination. Study authors identified a NOAEL of 500 mg/kg/day for maternal toxicity presumably based on body weight effects, and a NOAEL of 1,000 mg/kg/day for fetal effects based on reduced fetal body weight.
  - *Dermal:* *<u>Surrogate: Hydrodesulfurized kerosene (CAS #64742-82-1):</u>* In the previously described reproduction / developmental toxicity screening study conducted according to OECD Guideline 421, hydrodesulfurized kerosene was administered dermally to male and female Sprague-Dawley rats (10/sex) at doses of 0, 165, 330, or 494 mg/kg/day. Animals were treated 14 days prior to mating and continued through 2 weeks of mating and 20 days of gestation. There were no effects on mating, litter size, offspring body weights or offspring survival. Authors identified a NOAEL of 494 mg/kg/day which was the highest dose tested. No additional details were provided.
  - *Inhalation:* *<u>Surrogate: C9-12 isoalkanes (CAS #90622-57-4):</u>* In a prenatal developmental toxicity study conducted similar to OECD Guideline 414, pregnant female Sprague-Dawley rats (25/dose) were exposed to C9-12 isoalkanes vapor via inhalation at concentrations of 0, 300, or 900 ppm, 6 hours/day during gestation days 6 to 15. No treatment related effects were reported on fetal size, sex distribution, ossification variation, or fetal examination endpoints. Pregnancy rate, mortality, body weight gain, and gross postmortem observations were unaffected by treatment. Authors identified a NOAEC of 900 ppm (equivalent to

5,220 mg/m^3 as calculated by the authors) for maternal and developmental toxicity.
  - *Inhalation:* *<u>Surrogate: C9-C11, isoalkanes, cyclics (CAS #64742-48-9):</u>* In a prenatal developmental toxicity study conducted similar to OECD Guideline 414, pregnant female Sprague-Dawley rats (25/dose) were exposed to C9-C11, isoalkanes, cyclics vapor via inhalation at doses of 0, 300, or 900 ppm, 6 hours/day during gestation days 6 to 15. No treatment related effects were reported on fetal size, sex distribution, ossification variation, or fetal examination endpoints. Pregnancy rate, mortality, body weight gain, and gross postmortem observations were unaffected by treatment. Authors identified a NOAEC of 900 ppm (equivalent to 5,220 mg/m^3 as calculated by the authors) for maternal and developmental toxicity.
- ECHA CHEM, CAS #13475-82-6, 2024
  - *Inhalation:* *<u>Surrogate: Stoddard solvent IIC (CAS #64742-88-7):</u>* In a GLP-compliant reproductive/developmental toxicity screening test similar to OECD Guideline 421, Sprague-Dawley rats (10 males and 40 females/dose) received whole body inhalation exposures to the vapor of a mixture of aromatic, paraffinic and naphthenic hydrocarbons with the tradename VARSOL 40 and sample name MRD-78-25 at 0, 100, or 300 ppm 6 hours per day, 5 days per week for 8 weeks. The supplier indicates that the mixture is similar to CAS # 64742-88-7 (Stoddard solvent) (Exxon Company 1979). After the exposure period, each male mated for one week each with two females, and the females were terminated 18 days after the beginning of mating. Offspring were evaluated for clinical signs, mortality, body weight, and gross pathology. There were no treatment-related effects on any of the parameters examined. Study authors identified a NOAEC of 300 ppm (equivalent to 1.72 mg/L according to ECHA dossier authors) for reproductive toxicity for this study (Klimisch 1, reliable without restriction).

Endocrine Activity (E) Score (H, M, or L): DG
Isododecane 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 present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- No data were identified.

<u>Group II and II* Human Health Effects (Group II and II* Human)</u>
Note: Group II and Group II* endpoints are distinguished in the v 1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen® Guidance v1.4, Annex 2 for more details.

Acute Mammalian Toxicity (AT) (Group II) Score (vH, H, M, or L): L
Isododecane was assigned a score of Low for acute toxicity based on oral and dermal LD_{50} values > 2,000 mg/kg and inhalation LC_{50} values exceeding the highest attainable concentration in multiple species on the target chemical and surrogates. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are > 2,000 mg/kg an inhalation LC_{50} values are > 20 mg/L vapor and 5 mg/L mist (CPA 2018b). The confidence in the score is high as it is based on experimental data from studies on the target chemical and surrogates across all routes of exposure.
- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.

- CIR 2012 (Note: inhalation studies reported by CIR (2012) did not include the tested forms of the substances (i.e. aerosol or vapor))
  - *Oral:* Isododecane had an oral LD_{50} (mice) > 2,000 mg/kg (no additional details).
  - *Oral:* *Surrogates:* Other isoparaffin mixtures had oral LD_{50} values >10,000 mg/kg in rats.
  - *Inhalation:* *Surrogate: C11-13 isoparaffins (CAS #N/A):* Tradename Isopar L, 4h LC_{50} > 5.01 mg/L in rats.
  - *Inhalation:* *Surrogate: C10-13 isoparaffins (CAS # N/A):* Tradename Soltrol 130, 6h LC_{50} > 8.2 mg/L in rats.
  - *Inhalation:* *Surrogate: C9-12 isoparaffins (CAS # N/A):* Tradename Shell Sol 71, 4h LC_{50} > 3.83 mg/L in rats.
  - *Inhalation:* *Surrogate: C10-13 isoparaffins (CAS # N/A):* Tradename Soltrol 130, 4h LC_{50} > 8.4 mg/L in dogs.
  - *Inhalation:* *Surrogate: C10-13 isoparaffins (CAS # N/A):* Tradename Soltrol 130, 6h LC_{50} > 14.2 mg/L in dogs.
  - *Inhalation:* *Surrogate: C10-13 isoparaffins (CAS # N/A):* Tradename Soltrol 130, 4h LC_{50} > 9.9 mg/L in guinea pigs.
  - *Inhalation:* *Surrogate: C10-13 isoparaffins (CAS # N/A):* Tradename Soltrol 130, 6h LC_{50} > 11.6 mg/L in monkeys.
- ECHA CHEM, CAS #13475-82-6, 2024
  - *Dermal:* *Surrogate: Paraffins (petroleum), normal C5-20 (CAS #64771-72-8):* Tradename Petrepar 134 (50/50), LD_{50} > 2,000 mg/kg in rats (GLP) (Klimisch 2, reliable with restrictions).
  - *Dermal:* *Surrogate: C10-12 normal paraffins (CAS #N/A):* LD_{50} = 5,730 mg/kg in unspecified animal species (non-GLP) (Klimisch 2, reliable with restrictions).
  - *Dermal:* *Surrogate: C12-14 normal paraffins (CAS #N/A):* LD_{50} > 2,000 mg/kg in rabbits (non-GLP) (Klimisch 2, reliable with restrictions).
  - *Dermal:* *Surrogate: C10-14 paraffins (CAS #93924-07-3):* LD_{50} > 2,000 mg/kg in rats (GLP) (Klimisch 2, reliable with restrictions).
  - *Dermal:* *Surrogate: Paraffins (petroleum), normal C5-20 (CAS #64771-72-8):* Tradename Petrepar 134 (60/40), LD_{50} > 2,000 mg/kg in rats (GLP) (Klimisch 2, reliable with restrictions).
  - *Dermal:* *Surrogate: Paraffins (petroleum), normal C5-20 (CAS #64771-72-8):* Tradename Petrepar 100-Q, LD_{50} > 2,000 mg/kg in rats (GLP) (Klimisch 2, reliable with restrictions).
- OECD 2012
  - *Inhalation:* *Surrogate:* Members of the C9-C14 aliphatic hydrocarbon solvents (< 2% aromatics) category have low acute inhalation toxicity demonstrated by the LC_{50} values greater than the highest attainable vapor concentrations.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-single) (Group II) Score (vH, H, M, or L): *H*

Isododecane was assigned a score of High for systemic toxicity (single dose) based on a non-harmonized classification of H304 - May be fatal if swallowed and enters airways and because it is a hydrocarbon with a kinematic viscosity is below the cutoff of 20.5 mm^2/s for classification as a Category 1 aspiration hazard. GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (single dose) when they are classified as Category 1 aspiration hazard with the hazard statement H304 ((CPA 2018b). The confidence in the score is low as it is based on a non-harmonized classification and because details about the viscosity value are not available.

- Authoritative and Screening Lists

- *Authoritative:* Not present on any authoritative lists for this endpoint.
- *Screening:* H304 - May be fatal if swallowed and enters airways (EU, non-harmonized).

- ECHA C&L 2024
  - Isododecane was classified as a Category 1 aspiration hazard (H304) by the majority of notifiers to ECHA.
- Making Cosmetics 2020
  - Isododecane has a kinematic viscosity of 0.052 cm^2/s (5.2 mm^2/s) (temperature unspecified)
    - *Hydrocarbons with a kinematic viscosity < 20.5 mm^2/s at 40°C are classified as Category 1 aspiration hazards under GHS criteria (UN 2023). Isododecane has a kinematic viscosity of 5.2 mm^2/s at an unspecified temperature. Although the temperature was not reported, viscosity is typically measured at temperatures of 20°C or higher (OECD 2012b). Therefore, the kinematic viscosity at 40°C is expected to be 5.2 mm^2/s or less (viscosity will decrease with increasing temperature), which is well below the cutoff of 20.5 mm^2/s for classification.*
- ECHA CHEM, CAS #540-84-1, 2024
  - *Oral: <u>Surrogate: Isooctane (CAS #540-84-1):</u>* In an acute oral toxicity study on isooctane, Sprague-Dawley rats (5/sex) received a single gavage dose of 5,000 mg/kg and were observed for 14 days. There was no mortality during the observation period. Eight of the 10 animals showed depression, salivation, wheezing, rough coat, and soft feces one hour after exposure, but all animals appeared normal from day 2 onwards. All animals gained weight during the study and there were no abnormal gross pathological findings (Klimisch 2, reliable with restrictions).
  - *Dermal: <u>Surrogate: Isooctane (CAS #540-84-1):</u>* In a GLP-compliant acute dermal toxicity study, New Zealand White rabbits (3/sex) received unchanged isooctane (100% purity) on the skin at 2,000 mg/kg for 24 hours (type of coverage not reported). They were then observed for 14 days before necropsy. No animals died during the observation period, and animals gained weight during the study. Very slight erythema, which was completely reversible by day 7, was observed in all animals. Very slight edema that was completely reversible by day 3 was found in 3 animals. One animal had epidermal scaling on day 10. There were no gross pathological findings upon necropsy (Klimisch 2, reliable with restrictions).
  - *Inhalation: <u>Surrogate: Isooctane (CAS #540-84-1):</u>* In a GLP-compliant acute toxicity study performed according to OECD Guideline 403 in Sprague-Dawley rats, animals (5/sex) were exposed to isooctane vapor (100% purity) by whole-body inhalation at 33.52 mg/L for 4 hours and observed for 14 days. No animals died during the observation period. All animals lied prostrate in the cage and displayed rapid respiration during exposure, but returned to normal after exposure. Males had slightly decreased body weight on day 2 post exposure and females had slightly decreased body weight on days 2 to 4 post exposure. There were no gross pathology findings upon necropsy (Klimisch 2, reliable with restrictions).

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-repeat) (Group II*) Score (H, M, or L): L

Isododecane was assigned a score of Low for systemic toxicity (repeated dose) based on a subchronic oral NOAEL of 330 mg/kg/day in rats and a subchronic inhalation NOEC of 9 mg/L/6h/day vapor. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when the oral NOAEL is > 100 mg/kg/day and the inhalation NOAEC is > 1.0 mg/L/6h/day vapor (CPA 2018b). The confidence in the score is high as it is based on reliable data on the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- Health Canada 2022
    - *Oral:* In a subchronic toxicity study (guideline and GLP unspecified), Wistar rats (20/sex/dose) received isododecane (vehicle unspecified) by gavage at 0, 330, 1,000, or 3,000 mg/kg/day for 13 weeks. Effects at the low dose included decreased α-globulin levels and increased absolute/relative liver, spleen, and kidney weights, slight to mild degeneration with inflammation and tubular degeneration in male kidneys. Clinical chemistry changes included increased urea, protein, albumin, glutamic oxaloacetic transaminase, calcium levels and decreased α-, β-globulin levels, which Health Canada considered secondary to liver and kidney effects. Effects at the high dose. Hematological changes at the high dose included decreased erythrocyte, hemoglobin, and hematocrit, which remained within the range of historical controls. Additional endpoints evaluated, if any, were not specified. Health Canada notes that the effects associated with α2μ-globulin nephropathy in male rats are not relevant to humans, and therefore, they identified a NOAEL of 330 mg/kg/day and a LOAEL of 1,000 mg/kg/day based on degenerative changes in the liver.
    - *Inhalation:* In a subchronic inhalation toxicity study (guideline and GLP unspecified), rats (strain unspecified, 20/sex/dose) were exposed whole-body to isododecane vapor at concentrations of 0, 12.5, 50, 100, and 200 ppm (equivalent to 0, 87, 348, 697, or 1,393 mg/m^3) 6 hours per day, 5 days per week for 13 weeks. Examinations include clinical observation, growth, hematology, clinical chemistry, urinalysis, gross pathology on major organs, and histopathology of the kidneys. No adverse effects were reported other than α2μ-globulin nephropathy, which is male rat-specific, at 50 ppm and above. Therefore, ToxServices identified a NOAEC at 200 ppm, which is equivalent to 1.393 mg/L (0.995mg/L after adjusting for intermittent exposure).
    - *Inhalation:* In a subchronic inhalation toxicity study (guideline and GLP unspecified), rats (strain unspecified, 20/sex/dose) were exposed whole-body to isododecane vapor at concentrations of 0, 200, 600, and 1,800 ppm (equivalent to 0, 1,400, 4,200, 12,600 mg/m^3) 6 hours per day, 5 days per week for 13 weeks. No adverse effects were reported other than α2μ-globulin nephropathy, which is male rat-specific, in all treated groups. Therefore, ToxServices identified a NOAEC at 1,800 ppm, which is equivalent to 12.6 mg/L (9 mg/L after adjusting for intermittent exposure).
- OECD 2012a
    - *Oral:* *<u>Surrogate: Multiple (CAS #N/A):</u>* The report briefly reviewed several subchronic oral toxicity studies of C9-C14 aliphatic category members and supporting chemicals, including branched alkanes with carbon lengths between 10 and 13. All tests were performed in manners similar or equivalent to currently established OECD guidelines (408 or 422) and the test substances were administered via gavage. No signs of toxicity were observed at the maximum experimental dose tested, 5,000 mg/kg/day. In some studies liver weights increased without corresponding changes in liver enzymes and effects resolved after 28-day recovery periods. Kidney effects were seen in male rats exposed to lower molecular weight solvents and were attributed to an α2μ-globulin mediated response that is not relevant to human health.

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

Isododecane was assigned a score of Moderate for neurotoxicity (single dose) based on reversible narcotic effects after acute oral and inhalation exposure to a surrogate in rats and mice, which warrants

GHS Category 3 classification. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when they are classified as GHS Category 3 (CPA 2018b). The confidence in the score is low as the most robust study data are from a weaker surrogate.

- 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 CHEM, CAS #540-84-1, 2024
    - *Oral:* *<u>Surrogate: Isooctane (CAS #540-84-1):</u>* In an acute oral toxicity study on isooctane, Sprague-Dawley rats (5/sex) received a single gavage dose of 5,000 mg/kg and were observed for 14 days. There was no mortality during the observation period. Eight of the 10 animals showed depression, salivation, wheezing, rough coat, and soft feces one hour after exposure, but all animals appeared normal from day 2 onwards. All animals gained weight during the study and there were no abnormal gross pathological findings (Klimisch 2, reliable with restrictions).
    - *Dermal:* *<u>Surrogate: Isooctane (CAS #540-84-1):</u>* In a GLP-compliant acute dermal toxicity study, New Zealand White rabbits (3/sex) received unchanged isooctane (100% purity) on the skin at 2,000 mg/kg for 24 hours (type of coverage not reported). They were then observed for 14 days before necropsy. No animals died during the observation period, and there were no gross pathological findings upon necropsy (Klimisch 2, reliable with restrictions).
    - *Inhalation:* *<u>Surrogate: Isooctane (CAS #540-84-1):</u>* In a GLP-compliant acute toxicity study performed according to OECD Guideline 403 in Sprague-Dawley rats, animals (5/sex) were exposed to isooctane vapor (100% purity) by whole-body inhalation at 33.52 mg/L for 4 hours and observed for 14 days. No animals died during the observation period. All animals lied prostrate in the cage and displayed rapid respiration during exposure, but returned to normal after exposure. There were no gross pathology findings upon necropsy (Klimisch 2, reliable with restrictions).
- ECHA CHEM, CAS #13475-82-6, 2024
    - *Inhalation:* *<u>Surrogate: Multiple (CAS #N/A):</u>* The potential for acute neurotoxicity of C9-C11 and C10-C12 isoparaffinic solvents was tested in CFW mice that were exposed to vapors in operant conditioning chambers for 30 minutes. Locomotor activity and the ability to respond in tests of schedule-controlled operant behavior were assessed. C7-8, C8-9, and C10-11 isoparaffins produced reversible increases in locomotor activity of mice at 4,000 and 6,000 ppm (equivalent to 23.231 and 34.846 mg/L) and reversible decreases in rates of schedule controlled operant behavior in the same concentration range. The locomotor activity and operant behavior NOAEC for C7-8, C8-9, and C10-11 isoparaffins was determined to be 1,000 ppm. The locomotor activity and operant behavior NOAEC for C11-12 isoparaffins was determined to be >2,000 ppm. There were no treatment related effects in mice exposed to C10-C12 solvent, but authors noted that it was difficult to produce high vapor concentrations of this compound (Klimisch 1, reliable without restriction)
- OECD 2012a
    - *Inhalation:* *<u>Surrogate: Multiple (CAS #N/A):</u>* Members of the C9-C14 aliphatic hydrocarbons category with carbon numbers up to approximately 10 may cause acute, reversible CNS effects. Hydrocarbons with carbon numbers greater than 10 do not produce CNS effects at the maximum attainable concentrations, as they are not completely volatilized.

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

Isododecane was assigned a score of Low for neurotoxicity (repeated dose) based on an adjusted inhalation NOAEC of 17.3 mg/L/6h/day and an oral NOAEL of 1,000 mg/kg/day in studies on surrogates. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when the inhalation NOAEC is > 1 mg/L/6h/day (CPA 2018b). The confidence in the score is low as there were some potential concerns reported in humans for the surrogate white spirits.

- 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 CHEM, CAS #124-18-5, 2024
    - *Oral: Surrogate: Decane (CAS #124-18-5):* In a GLP-compliant combined reproduction and developmental toxicity screening test conducted in a manner similar to OECD Guideline 422 in 1995, Sprague-Dawley rats (10/sex/dose) were administered surrogate decane (97% purity) at doses of 0, 25, 150, or 1,000 mg/kg/day via gavage for 14 days prior to mating, through the mating period, and for a total of 46 days (males) or through lactation day 4 (females). There were no test-related findings in neurobehavioral activity. Functional tests including startle reflex, open field test, and forelimb grip reflex performance were evaluated, and no treatment-related effects were observed. Additionally, histopathology and gross pathology findings did not report treatment related effects of the brain or spinal cord. Study authors identified a NOAEL of 1,000 mg/kg/day, the highest dose tested, for systemic toxicity, including neurotoxicity (Klimisch 1, reliable without restrictions).
- OECD 2012a
    - OECD summarized a review of human literature demonstrating the potential for hydrocarbon solvents to cause chronic neurological effects in humans. The review focused on IPCS, SCOEL, and ECHA Committee for Risk Assessment evaluations of epidemiological studies of white spirits, which is a C9-C11 aliphatic hydrocarbon solvent containing 15-20% aromatics. In epidemiological studies, this solvent has been associated with complaints of memory fatigue, impaired concentration, irritability, dizziness, headache, anxiety and apathy, and impairment in short-term visual memory tests and the symbol-digit test. Effects increased with duration of exposure. ECHA's RAC concluded that chronic exposure to white spirits can cause effects in psychomotor, perception, and memory parameters, and disturbances in mood which can progress in severity. Studies are confounded by co-exposure to other solvents __
    - *Inhalation: Naphtha (petroleum), heavy alkylate (CAS #64741-65-7):* In a 13-week study, rats were exposed to 668, 2,220, or 6,646 ppm (2.4, 8.1, or 24.3 mg/L) alkylate naphtha distillate vapor containing C5-C8 isoparaffinic hydrocarbons for 6 hours/day, 5 days/week for 13 weeks via whole body inhalation. Evaluations of motor activity and functional observation battery were performed on weeks 5, 9, 14, and 18 (in a recovery group). Nervous tissue was also evaluated in 6 animals/group. No additional experimental details were provided. There were no treatment-related effects in the functional observation battery. Effects on motor activity (not described) were considered by authors to be indicative of acute CNS depression rather than cumulative neurotoxicity. There were no effects on pathology of the brain, spinal cord, or peripheral nerves. Authors identified a NOAEC of 24.3 mg/L/6h for neurotoxicity, equivalent to 17.3 mg/L/6h/day after adjustment for a daily treatment frequency).
- Based on the weight of evidence, a score of Low was assigned. While human data on white spirits indicate a potential for neurotoxicity concerns, as noted by OECD, it is not clear if isododecane or other hydrocarbon compounds in the mixture, including the 15-20% aromatics, contributed to the observed neurotoxicity. The combined reproduction and developmental toxicity screening test in

rats on surrogate decane did not identify neurotoxicity in neurobehavioral assessments, functional tests, and organ weights, gross pathology, and histopathology of neuronal tissues. Additionally, the inhalation study on alkylate naphtha distillate vapor did not identify neurotoxicity. Due to the uncertainty regarding the contribution of aromatic compounds to effects reported in humans, ToxServices relied most heavily on the high quality study for the study on decane, which was conducted with high purity test substance. Therefore, isododecane is GHS Not Classified based on the NOAEL of 1,000 mg/kg/day, which is above the duration-adjusted GHS cutoff of 200 mg/kg/day for Category 2, and an adjusted inhalation NOAEC of 17.3 mg/L/6h/day, which is above the GHS cutoff of 1 mg/L/6h/day for Category 2.

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

Isododecane was assigned a score of Low for skin sensitization based on multiple human studies demonstrating no skin sensitization. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when there is adequate negative data (CPA 2018b). The confidence in the score is high as it is based on reliable data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- CIR 2012
  - In a safety-in-use study of a hair oil mist spray containing 90.3% isododecane, 69 male and female volunteers used the product for 6 consecutive weeks and were then dermally challenged 10 to 14 days after the last use of the product. There were no skin sensitization reactions in this study.
  - Results in 108 participants (male and female) were negative for skin irritation and sensitization following use of a lip primer containing 80.74% isododecane.
  - Results in 104 participants (male and female) were negative for skin irritation and sensitization following use of an eye shadow containing 47.64% isododecane.
  - Results in 108 participants (male and female) were negative for skin irritation and sensitization following use of an eyeliner containing 40.16% isododecane. One hundred of the subjects participated in the challenge phase.
  - Results in 204 participants (male and female) were negative for skin irritation and sensitization following use of mascara containing 63.7% isododecane.
  - Results in 52 participants (male and female) were negative for skin irritation and sensitization following patch applications of permethyl 296C (50% isododecane).
  - Results in 52 participants (male and female) were negative for skin irritation and sensitization following patch applications of permethyl 284C (20% isododecane). One participant had a barely perceptible reaction post challenge that was considered not clinically significant, and one participant had a moderate reaction. Authors concluded the test substance was not irritating or sensitizing.

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*

Isododecane was assigned a score of Low for respiratory sensitization based on lack of structural alerts and extrapolation of skin sensitization results. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when they are GHS Not Classified (CPA 2018b). Confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- 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 2024
  - Isododecane does not contain any structural alerts for respiratory sensitization (Appendix G).
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As isododecane was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by isododecane, and as isododecane does not contain any structural alerts for respiratory sensitization (OECD 2024), isododecane is not expected to be a respiratory sensitizer.

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

Isododecane was assigned a score of High for skin irritation/corrosivity based on a GHS Category 2 classification from a rabbit study on a surrogate. GreenScreen® criteria classify chemicals as a High hazard for skin irritation/corrosivity when they are GHS Category 2 (CPA 2018b). The confidence in the score is low as the severity of skin irritation varies across two animal studies, and poorly reported studies on the target suggest at most mild irritation.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- CIR 2012
  - Isododecane was not irritating to 20 human volunteers in an open patch test at ~85% concentration. It was irritating to the skin in a closed patch test in another 20 human volunteers at 10% (2 participants), 20% (3 participants) and 50% (6 participants) in petrolatum. In a third study, skin irritation was observed in 2 of 19 participants tested with 40% isododecane and 60% trimethylsiloxysilicate with closed patches at 40% in petrolatum (i.e. isododecane tested at 16%).
  - Undiluted isododecane was mildly irritating to the skin of 6 rabbits in a 24-hour contact period test. No additional details were provided.
  - Undiluted isododecane was mildly irritating to the skin of 3 rabbits in a cumulative irritation test. No additional details were provided.
  - Isododecane (50% in petrolatum) was mildly irritating to the skin of 3 rabbits in a primary irritation test. No additional details were provided.
- ECHA CHEM, CAS #13475-82-6, 2024
  - <u>*Surrogate: Hydrocarbons, C10-12 isoalkanes, with <2% aromatics (CAS #N/A):*</u> In a GLP-compliant dermal irritation study conducted similar to OECD Guideline 404, three male New Zealand white rabbits were exposed to 0.5 mL unchanged test substance, (tradename MRD-00-710) on shaved skin under semi-occlusion for 4 hours and observed for 14 days. The mean erythema score for all three animals across 24, 48 and 72 hours was 2.33, and the mean edema score was 1.1. The effects were reversible. Scores for the individual animals were not reported. Authors of the REACH dossier concluded that the test substance was a Category 2 dermal irritant (Klimisch 1, reliable without restriction). *Mean scores of $\geq$ 2.3 and $\leq$ 4.0 for erythema and/or edema in 2/3 animals corresponds to GHS Category 2 (UN*

2023). Although individual animal scores were not provided, a mean of 2.33 for erythema suggests that the individual score was likely > 2.3 in at least two animals.

  - *Surrogate: Hydrocarbons, C10-12 isoalkanes, with <2% aromatics (CAS #N/A):* In another GLP-compliant dermal irritation study conducted similar to OECD Guideline 404 with three New Zealand White rabbits, the mean 24/48/72 hour scores following a 4 hour semi-occlusive application were 1.3, 1.3, and 2.0 for erythema and 0, 0, and 0 for edema. *Mean scores of > 1.5 and < 2.3 for erythema and/or edema in 2/3 animals corresponds to GHS Category 3. Therefore, the substance is not classified based on results of this study.*
- Based on the weight of evidence, a score of High was conservatively assigned. The surrogate hydrocarbons, C10-12, isoalkanes, <2% aromatics produced mixed results intro reliable rabbit studies, was with one supporting it not being classified and the other supporting it being classified to GHS Category 2. Results ranged from non-irritating to irritating to the skin of humans (CIR 2012). ToxServices conservatively classified undecane as GHS Category 2 based on the results of one animal study with support from human data suggesting the potential for irritation.

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

Isododecane was assigned a score of Low for eye irritation/corrosivity based on negative results in rabbit studies. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when negative data and no GHS classification are available (CPA 2018b). The confidence in the score is high as experimental data is available on the target chemical and the results are supported by a reliable study on a surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- CIR 2012
  - Isododecane (tradename Permethyl 284C and Permethyl 296C) was non-irritating in two Hen's egg tests *in vitro*. No additional details were provided.
  - Isododecane was also non-irritating in three studies in rabbits. No additional details were provided.
- ECHA CHEM, CAS #13475-82-6, 2024
  - *Surrogate: Hydrocarbons, C10-12 isoalkanes, with <2% aromatics (CAS #N/A):* In a GLP-compliant eye irritation study conducted according to OECD Guideline 405, three New Zealand white rabbits were exposed to 0.1 mL unchanged test substance, (tradename Sample V) in the eye and observed for 72 hours afterwards. Mean 24 – 72 hours scores for conjunctival redness, chemosis, corneal opacity and iritis were 0 for all animals. Authors of the REACH dossier concluded that the test substance was not irritating to the eye (Klimisch 1, reliable without restriction).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L

Isododecane was assigned a score of Low for acute aquatic toxicity based on no effects at saturation in fish, daphnia, and algae studies. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when they are GHS Not Classified (CPA 2018b). The confidence in the score is high as it is based on experimental data for all three trophic levels.

- 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 CHEM, CAS #13475-82-6, 2024
    - Isododecane 48h LL_{50} (> 1,000 mg/L (nominal), 96h LC_{50} > 2.8 µg/L (measured) (GLP, OECD Guideline 203) (Klimisch 1, reliable without restriction)
    - Isododecane 48h EL_{50} (*Daphnia magna*) > 90% saturated solution in water (GLP, DIN 38412 Part I) (Klimisch 2, reliable with restrictions).
    - Isododecane 72h EC_{50} (*Desmodesmus subspicatus*, green algae) > 22.5 µg/L (measured, highest tested concentration, approaching saturation) based on cell number and growth rate, (GLP, OECD Guideline 201) (Klimisch 1, reliable without restriction).
- U.S. EPA 2022
    - Isododecane belongs to the Neutral Organics ECOSAR chemical class. The most conservative predicted acute E/LC_{50} values are 0.026 mg/L in fish (96h), 0.021 mg/L in daphnia (48h), and 0.078 mg/L in green algae (96h) (Appendix H). *Note that the predictions for fish and daphnia are flagged for exceeding log K_{ow}, and all three predicted values are greater than the expected water solubility of isododecane (insoluble). No effects are expected at saturation.*

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): vH
Isododecane was assigned a score of Very High for chronic aquatic toxicity based on a NOEC of 0.013 mg/L in daphnia. GreenScreen® criteria classify chemicals as a Very High hazard for chronic aquatic toxicity when they have chronic NOEC values < 0.1 mg/L (CPA 2018b). The confidence in the score is high as it is based on experimental data and supported by modeling.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* H413 - May cause long lasting harmful effects to aquatic life.
- ECHA CHEM, CAS #13475-82-6, 2024
    - Isododecane 21d NOEC (*D. magna*) = 0.013 mg/L and LOEC = 0.029 mg/L based on immobility and reproduction. The authors note that these values are based on the time-weighted mean measured test concentration and that there were challenges due to the insolubility of the test substance and possible loss through volatility (GLP, OECD Guideline 211) (Klimisch 1, reliable without restriction).
    - Isododecane 72h NOEC (*D. subspicatus*, green algae) = 22.5 µg/L (measured, highest achievable tested concentration, approaching saturation) based on cell number and growth rate (GLP, OECD Guideline 201) (Klimisch 1, reliable without restriction).
- U.S. EPA 2022
    - Isododecane belongs to the Neutral Organics ECOSAR chemical class. The most conservative predicted chronic values (ChVs) are 0.0040 mg/L in fish, 0.0061 mg/L in daphnia, and 0.048 mg/L in green algae (Appendix H).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *L*
Isododecane was assigned a score of Low for persistence based on surrogate studies demonstrating it meets the pass level but fails the 10-day window in ready biodegradability tests and has a modeled half-life of 15 days in water. GreenScreen® criteria classify chemicals as a Low hazard for persistence when they are classified as GHS rapid degradability or have a half-live < 16 days in water (CPA 2018b). The confidence in the score is low as it is based on a modeled half-life and the data conflict across 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.

- ECHA CHEM, CAS #13475-82-6, 2024
    - *<u>Surrogate: Hydrocarbons, C12-13 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C12-13 isoalkanes and cyclics with <2% aromatics was degraded by 7.3, 16.2, 50.4, 60.02, and 89.8% by 4, 5, 13, 16 and 28 days, respectively, in a GLP-compliant OECD Guideline 301F study. Therefore, it is readily biodegradable but fails the 10-day window (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: Hydrocarbons, C12-16 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C12-16 isoalkanes and cyclics with <2% aromatics was degraded by 10.5, 22.4, 43.4, and 50.1% by 18, 28, 56, and 70 days, respectively, in a non-GLP-compliant OECD Guideline 301F study. Therefore, it is not readily biodegradable, but inherently biodegradable (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: Hydrocarbons, C10-12 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C10-12 isoalkanes and cyclics with <2% aromatics was degraded by 31.3, 40.5, 41.7, and 47.5% by 28, 41, 28, and 41 days, respectively, in a non-GLP-compliant OECD Guideline 301F study. Therefore, it is not readily biodegradable, but inherently biodegradable (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: C13 normal paraffins (CAS #N/A):</u>* Normal C13 paraffin was degraded by 32.3, 50.9, 64.4, 83.1, and 85.5% by 3, 5, 10, 28, and 32 days, respectively, in a non-GLP-compliant OECD Guideline 301F study. Therefore, it is readily biodegradable and meets the 10-day window (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: C11 and C12 normal paraffins (CAS #N/A):</u>* Normal C11 and C12 paraffins were degraded by 10, 50, 61.3, 76.6, and 76.6% by 3, 9, 12, 28, and 32 days, respectively, in a GLP-compliant OECD Guideline 301F study. Therefore, the test substance is readily biodegradable and meets the 10-day window (Klimisch 1, reliable without restriction).
    - *<u>Surrogate: Hydrocarbons, C12-16 n-alkanes, isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C12-16 n-alkanes, isoalkanes and cyclics with <2% aromatics was degraded by 4.8, 12.7, 53, 60.2, and 67.6% by 2, 3, 12, 18, and 28 days, respectively, in a GLP-compliant OECD Guideline 301F study. Therefore, it is readily biodegradable, but fails the 10-day window (Klimisch 1, reliable without restriction).
    - *<u>Surrogate: Hydrocarbons, C10-12 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C10-12 isoalkanes and cyclics with <2% aromatics was degraded by 0, 2.47, 5.44, 7.34, and 8.74% by 3, 8, 16, 24, and 31 days, respectively, in a non-GLP-compliant EPA OTS 796.3100 study. Therefore, it not inherently biodegradable (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: Hydrocarbons, C10-14 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C10-14 isoalkanes and cyclics with <2% aromatics was degraded by 1.74, 5.66, 13.63, 16.07, and 18.39% by 3, 8, 16, 24, and 31 days, respectively, in a non-GLP-compliant EPA OTS 796.3100 study. Therefore, it not inherently biodegradable (Klimisch 2, reliable with restrictions).
    - *<u>Surrogate: Hydrocarbons, C12-13 isoalkanes and cyclics, <2% aromatics (CAS #N/A):</u>* Hydrocarbons, C12-13 isoalkanes and cyclics with <2% aromatics was degraded by 6.03, 8.69, 11.69, 12.69, and 13.69% by 3, 8, 16, 24, and 31 days, respectively, in a non-GLP-compliant EPA OTS 796.3100 study. Therefore, it not inherently biodegradable (Klimisch 2, reliable with restrictions).
- U.S. EPA 2017
    - The BIOWIN modeling Ready Biodegradable Predictor indicates that isododecane is

expected to be readily biodegradable. Fugacity modeling (MCI method) predicts 70.9% will partition to water with a half-life of 15 days, 19.1% will partition to air with a half-life of 18.4 hours, 8.33% will partition to sediment with a half-life of 135 days, and 1.7% will partition to soil with a half-life of 30 days (Appendix I).

- Available experimental data on surrogates indicate that as chain lengths and degree of branching increase, the rate of biodegradation decreases. When conflicting but reliable data are reported for surrogates of similar composition, ToxServices weights studies that achieve higher degree of degradation more heavily, according to OECD Guidance (OECD 2001). Surrogates that contain mainly isoalkanes achieved pass levels in ready biodegradability studies but failed the 10-day window in best-performing studies. Modeled data with the more linear structure indicate ready biodegradability, as supported by data demonstrating that normal paraffins meet the 10-day window. The overall weight of evidence suggests that as a branched 12-carbon compound, isododecane is likely to meet the pass level in ready biodegradability studies, but fail the 10-day window. The modeled half-life of 15 days in water corresponds to a Low.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *H*

Isododecane was assigned a score of High for bioaccumulation based on a measured BCF values of 4,408 in a surrogate from a study that included dietary exposure. GreenScreen® criteria classify chemicals as a High hazard for bioaccumulation when BCF values are greater than 1,000 to 5,000 (CPA 2018b). The confidence in the score is low as it is based on surrogates that are moderately similar to isododecane.

- 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 2012a
  - <u>*Surrogate: Multiple (CAS #N/A):*</u> Some members of the C9-C14 aliphatic (≤2% aromatic) hydrocarbon solvents category have the potential to bioaccumulate. Measured BCF values of 400 (aqueous) to 4,408 (dietary) for n-dodecane in fathead minnow and rainbow trout and 1,468 for iso-nonanes in carp have been reported.
- U.S. EPA 2017
  - BCFBAF predicts a BCF of 227.9 L/kg wet-wt using the regression based model based on a modeled log K_{ow} of 6.16, and a BCF of 2,043 and a BAF of 7,892 using the Arnot-Gobas model for the upper trophic level, taking metabolism into consideration (Appendix I).
- Based on the weight of evidence, a score of High was assigned. Although some of the models predict BAF values > 5,000, and BAF estimates are preferred over BCF estimates for chemicals with high log K_{ow} values, experimental data in fish from OECD (2012) indicates measured BCF values ranging from 400 to 4,408, with the highest value obtained from a study that included dietary exposure for surrogates, which correspond to a score of High. The predicted BCF of 227.9 L/kg wet-wt (regression-based) corresponds to a score of Moderate, whereas the predicted BCF (Arnot-Gobas) of 4,408 corresponds to a high. Overall, ToxServices weighed the measured BCF of 4,408 from a study that included dietary exposure most heavily, and assigned a High..

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*

Isododecane was assigned a score of Low for reactivity based on lack or structural alerts / functional groups associated with reactivity. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are GHS Not Classified (CPA 2018b). The confidence in the score was low as there is no measured data available.

- 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 measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of isododecane. These procedures are listed in the GHS (UN 2023).
  - Based on the structure of its components or moieties, isododecane is not considered explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix J).
  - Based on the structure of its components or moieties, isododecane is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials. Specifically, organic substances which contain oxygen, fluorine, or chlorine where these elements are chemically bonded only to carbon or hydrogen, classification as an oxidizing liquid need not be applied. Therefore, as the molecular structure of isododecane has 0 oxygens, classification is not warranted.
- No data were identified.

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

Isododecane was assigned a score of Moderate for flammability based on a measured flash point ranging between 41 and 56.7°C, which is within the range of 23°C and 60°C for GHS Category 3. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when they are classified as GHS Category 3 (CPA 2018b). The confidence in the score was high as it is based on experimental data on the target chemical.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* H226 - Flammable liquid and vapor.
- CIR 2012
  - Isododecane has an experimental flash point of 56.7°C.
- ECHA CHEM, CAS #13475-82-6, 2024
  - Isododecane has an experimental flash point of 45°C according to Abel-Pensky closed cup method (DIN 51755) (Klimisch 2, reliable with restrictions).
  - Isododecane has an experimental autoflammability temperature of 41°C according to test method ASTM E659 (Klimisch 2, reliable with restrictions).

Use of New Approach Methodologies (NAMs)[12] in the Assessment, Including Uncertainty Analyses of Input and Output

New Approach Methodologies (NAMs) used in this GreenScreen® include *in vitro* testing for mutagenicity and eye irritation, and *in silico* modeling for carcinogenicity, respiratory sensitization, acute and chronic aquatic toxicity, persistence, and bioaccumulation. NAMs are non-animal alternative that can be used alone or in combination to provide information for safety assessment (Madden et al. 2020). At present, there is not a uniformly accepted framework on how to report and apply individual NAMs (U.S. EPA 2020, OECD 2020). The expanded application of NAMs greatly amplifies the need to communicate uncertainties associated with their use. As defined by EFSA (2018), uncertainty is "a general term referring to all types of limitations in available knowledge that affect the range and probability of possible answers to an assessment question." The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties (OECD 2020):

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

As shown in Table 5, Type I (input data) uncertainties in isododecane's NAMs dataset include lack of, or insufficient experimental data for carcinogenicity and respiratory sensitization, and lack of validated test methods for respiratory sensitization. Isododecane's Type II (extrapolation output) uncertainties include the lack of defined applicability domains of some modeling programs, limitations of *in vitro* genotoxicity assays in assessing only a few processes in genotoxicity and not completely mimicking *in vivo* metabolism, and respiratory sensitization alerts' lack of consideration of non-immunological mechanisms. Some of isododecane's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

Table 5: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses	
Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	**Carcinogenicity**: No experimental data are available. **Respiratory sensitization**: No experimental data are available and there are no validated test methods. **Chronic aquatic toxicity:** Measured data are not available for all trophic levels.
Type II Uncertainty: Extrapolation Output	**Carcinogenicity**: Toxtree only identifies structural alerts (SAs), and no applicability domain can be defined (Toxtree 2018). **Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[13]. The mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous

[12] NAMs refers to any non-animal technology, methodology, approach, or combination thereof that inform chemical hazard and risk assessments. NAMs include *in silico*/computational tools, *in vitro* biological profiling (e.g., cell cultures, 2,3-D organotypic culture systems, genomics/transcriptomics, organs on a chip), and frameworks (i.e., adverse outcome pathways (AOPs), defined approaches (DA), integrated approaches to testing and assessment (IATA).
[13] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427

	metabolic activation system does not entirely mirror *in vivo* metabolism (i.e., the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).[14] The *in vitro* chromosome aberration assay (OECD Guideline 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[15]. **Respiratory sensitization**: The OECD Toolbox only identifies structural alerts, and does not define applicability domains. Additionally, the ECHA guidance (2017), on which the use of OECD Toolbox structural alerts is based, does not evaluate non-immunologic mechanisms for respiratory sensitization.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	Y	*In silico* modeling: VEGA/Toxtree/ Danish QSAR
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/*in vitro* gene mutation assay/*in vitro* chromosome aberration assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	N	
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	N	
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™

[14] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE
[15] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352

		Non-animal testing: OECD 301 F Biodegradation tests
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

References

ChemSrc. 2024. Isododecane (CAS #31807-55-3). Available: https://www.chemsrc.com/en/cas/31807-55-3_88494.html

Clean Production Action (CPA). 2018a. GreenScreen® Assessment Expiration Policy. October 2, 2018.

Clean Production Action (CPA). 2018b. The GreenScreen® for Safer Chemicals Guidance. Version 1.4 Guidance. Dated January, 2018. Available: https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1_4_2018_01_Final.pdf

Cosmetic Ingredient Review (CIR). 2012. Safety assessment of isoparaffins as used in cosmetics. *Int. J. Toxicol.* 31(supple. 3): 269S-295S. Available: https://cir-reports.cir-safety.org/view-attachment/?id=ee0fa771-8e74-ec11-8943-0022482f06a6

Cosmetics Business. 2012. Silicones & alternatives – spoilt for choice. Available: https://cosmeticsbusiness.com/silicones-alternatives-spoilt-for-choice-74765

Danish Technical University (DTU). 2024. National Food Institute. Danish QSAR Database. Available: http://qsar.food.dtu.dk/.

European Chemicals Agency (ECHA). 2017. Guidance on information requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint specific guidance. Version 6.0. Dated: July 2017. Available: https://echa.europa.eu/documents/10162/17224/information_requirements_r7a_en.pdf/e4a2a18f-a2bd-4a04-ac6d-0ea425b2567f?t=1500286622893

European Chemicals Agency (ECHA). 2019. Opinion on an Annex XV dossier proposing restrictions on D4, D5 and D6. Committee for Risk Assessment (RAC), Committee for Socio-economic Analysis (SEAC). Available: https://echa.europa.eu/documents/10162/44c5f15a-a022-5084-762e-03bbb00599d5

European Chemicals Agency (ECHA) Classification and Labelling Inventory (C&L). 2024. Summary of classification and labelling for isododecane (CAS #31807-55-3). Available : https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/43894

European Chemicals Agency Chemicals Database (ECHA CHEM). 2024. REACH dossier for chemicals. Available : https://chem.echa.europa.eu/

European Commission (EC). 2024. CosIng database. Available: https://ec.europa.eu/growth/tools-databases/cosing/index.cfm?fuseaction=search.simple

European Food Safety Authority (EFSA). 2018. Guidance on uncertainty analysis in scientific assessments. *EFSA J.* 16(1): e05123. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7009727/

Gad, S. 2016. QSAR Tools for Drug Safety. Chapter 10. In, Drug Safety Evaluation. Third Edition. New York: Wiley. 209-224.

Health Canada. 2022. Screening assessment nonane, 2,2,4,4,6,8,8-heptamethyl-(heptamethylnonane). Available: https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/screening-assessment-heptamethylnonane.html

Madden, J.C., S.J. Enoch, A. Paini, and M.T.D. Cronin. 2020. A review of *in silico* tools as alternatives to animal testing: principles, resources, and applications. *Alt. Lab. Animals.* 1-27. Available: https://journals.sagepub.com/doi/pdf/10.1177/0261192920965977

Making Cosmetics. 2020. Safety data sheet for Isododecane. Dated 8/19/2020. Available: https://www.makingcosmetics.com/on/demandware.static/-/Sites-makingcosmetics-master/default/dw5d19c72b/msds/sds-isododecane.pdf

Millipore Sigma. 2024. Safety data sheet for isododecane (CAS #31807-55-3), Product Number 06753. Version 6.5. Revision date September 8, 2024. Available: https://www.sigmaaldrich.com/US/en/sds/sial/06753

Organisation for Economic Co-operation and Development (OECD). 2012a. SIDS Initial Assessment Profile for C9-C14 Aliphatic [≤2% aromatic] Hydrocarbon Solvents Category. CoCAM 3, 16-18 October 2012. Available at: http://webnet.oecd.org/Hpv/UI/handler.axd?id=df9ce638-7b33-43c0-8080-bdad8796e192

Organisation for Economic Co-operation and Development (OECD). 2012b. OECD Guideline for the Testing of Chemicals. 114: Viscosity of Liquids. Available: https://www.oecd.org/en/publications/2012/10/test-no-114-viscosity-of-liquids_g1g23f67.html

Organisation for Economic Co-operation and Development (OECD). 2020. Overview of Concepts and Available Guidance related to Integrated Approaches to Testing and Assessment (IATA), Series on Testing and Assessment, No. 329, Environment, Health and Safety, Environment Directorate. Available: https://www.oecd.org/chemicalsafety/risk-assessment/concepts-and-available-guidance-related-to-integrated-approaches-to-testing-and-assessment.pdf

Organisation for Economic Co-operation and Development (OECD). 2024. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 4.7. Available: https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm#Download_qsar_application_toolbox

Pharos. 2024. Pharos chemical and material library entry for isododecane (CAS #31807-55-3). Available: http://www.pharosproject.net/material/.

PubChem. 2024. Isododecane (CAS #31807-55-3). United States National Library of Medicine. Available: https://pubchem.ncbi.nlm.nih.gov/

Sahigara, F. 2007. Defining the Applicability Domain of QSAR models: An overview. Available: http://www.moleculardescriptors.eu/tutorials/T7_moleculardescriptors_ad.pdf

Santa Cruz Biotechnology. 2024. Isododecane (CAS 31807-55-3). Available: https://www.scbt.com/p/isododecane-31807-55-3

ToxServices. 2021. SOP 1.37: GreenScreen® Hazard Assessments. Dated: May 24, 2021.

Toxtree. 2018. Estimation of Toxic Hazard- A Decision Tree Approach v3.1.0. Available: http://toxtree.sourceforge.net.

United Nations (UN). 2023. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Tenth revised edition.

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available: 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: 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). 2017. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

United States Environmental Protection Agency (U.S. EPA). 2020. New Approach Methods Workplan. Office of Research and Development. Office of Chemical Safety and Pollution Prevention. EPA 615B20001. June 2020. Available: https://www.epa.gov/sites/default/files/2020-06/documents/epa_nam_work_plan.pdf

United States Environmental Protection Agency (U.S. EPA). 2022. ECOSAR 2.2. Washington, DC, USA. Available: http://www.epa.gov/oppt/newchems/tools/21ecosar.htm/.

United States Environmental Protection Agency (U.S. EPA). 2024a. Safer Chemical Ingredients List (SCIL). Available: https://www.epa.gov/saferchoice/safer-ingredients

United States Environmental Protection Agency (U.S. EPA). 2024b. Safer Choice Standard. Available: https://www.epa.gov/saferchoice/standard

Virtual Models for Evaluating the Properties of Chemicals within a Global Architecture (VEGA). 2024. Predictive Model Platform version 1.2.4. Available: https://www.vegahub.eu/download/vega-qsar-download/

APPENDIX A: Hazard Classification 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 Isododecane (CAS #31807-55-3)

TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table / **Table 2: Chemical Details**

			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
									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	Isododecane	31807-55-3	*L*	L	L	L	DG	L	*H*	L	*M*	*L*	L	*L*	*H*	L	L	*vH*	*L*	*H*	*L*	M

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Isododecane	2

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

Table 6

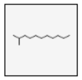
Chemical Name	Final GreenScreen® Benchmark Score
Isododecane	2

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 Isododecane (CAS #31807-55-3)



31807-55-3

Isododecane

ALSO CALLED 2-Methylhendecane, 250-816-8, 97659-99-9, DTXSID801010026, isodo-decane, Isododecane, ISODODECANE, I...

View all synonyms (9)

SHARE PROFILE

HAZARDS PROPERTIES FUNCTIONAL USES RESOURCES

All Hazards View

Show PubMed Results REQUEST ASSESSMENT ADD TO COMPARISON

		Group I Human					Group II and II* Human									Ecotox			Fate		Physical		Mult	Non-GSLT			
	GREENSCREEN®	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult	PBT	GW	O	Other
List Hazard Summary	LT-UNK	-	-	-	-	-	pC	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	U	-	-	-	R

Hazard Lists

DOWNLOAD LISTS

ENDPOINT	HAZARD LEVEL	GREENSCREEN®	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Acute Mammalian Toxicity	pC	NoGS	DK-EPA - Danish Advisory List	Acute Tox. 4 - Harmful if swallowed (modeled)	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-UNK	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters	

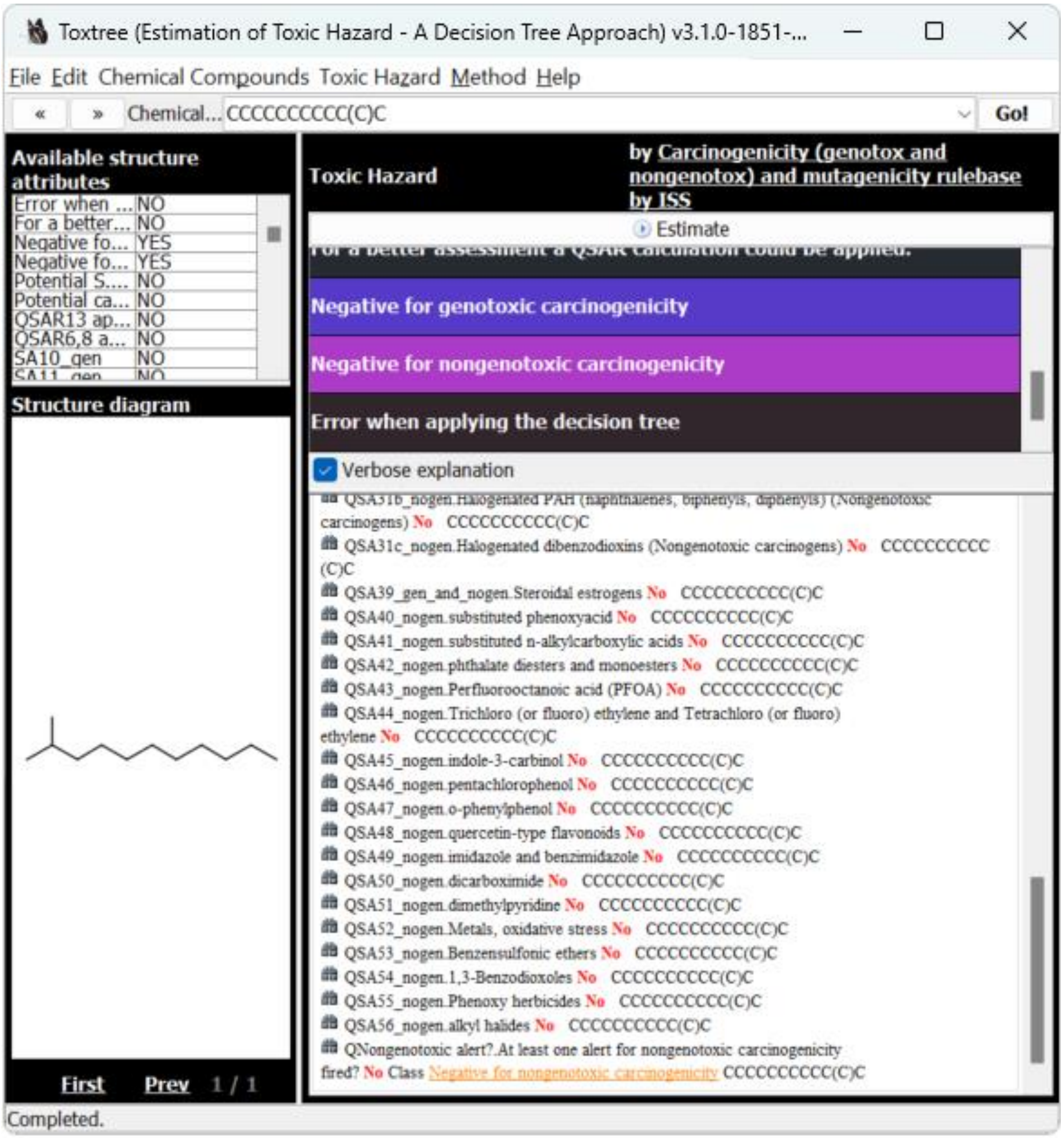
Restricted Substance Lists (3)

- Food Contact Chemicals Database (FCCdb): Food Contact Chemicals Database Version 5.0
- GSPI - Six Classes Precautionary List: Some Solvents
- TSCA Chemical Substance Inventory (Active-Inactive): TSCA Commercially Active

Positive Lists (2)

- Cosmetic Ingredient Review (CIR): Safe as Used
- Inventory of Existing Cosmetic Ingredients in China (IECIC 2021): Cosmetic Ingredients

APPENDIX D: Toxtree Carcinogenicity Results for Isododecane (CAS #31807-55-3)



APPENDIX E: VEGA Carcinogenicity Results for Isododecane (CAS #31807-55-3)

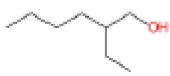
1. Prediction Summary

Prediction for compound Molecule 0 -

	Prediction: Reliability: Prediction is Carcinogen, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues: - Only moderately similar compounds with known experimental value in the training set have been found - Accuracy of prediction for similar molecules found in the training set is not adequate - similar molecules found in the training set have experimental values that disagree with the predicted value - predicted substance falls into a neuron that is populated by no compounds of the training set

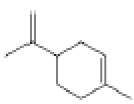
Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Carcinogen activity: Carcinogen
P(Carcinogen): 0.797
P(NON-Carcinogen): 0.203
Reliability: The predicted compound is outside the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 104-76-7
Dataset id:314 (Training Set)
SMILES: OCC(CC)CCCC
Similarity: 0.736
Experimental value : NON-Carcinogen
Predicted value : Carcinogen

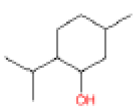


Compound #2

CAS: 5989-27-5
Dataset id:412 (Training Set)
SMILES: C=C(C)C1CC=C(C)CC1
Similarity: 0.731
Experimental value : Carcinogen
Predicted value : NON-Carcinogen

Compound #3

CAS: 111-68-2
Dataset id:357 (Test Set)
SMILES: NCCCCCCC
Similarity: 0.713
Experimental value : NON-Carcinogen
Predicted value : Carcinogen



Compound #4

CAS: 89-78-1
Dataset id:427 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.713
Experimental value : NON-Carcinogen
Predicted value : Carcinogen

Compound #5

CAS: 35449-36-6
Dataset id:345 (Training Set)
SMILES: OCC(C)(C)CCCCCCC(C)(C)CO
Similarity: 0.695
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #6

CAS: 1643-20-5
Dataset id:273 (Training Set)
SMILES: [O-][N+](C)(C)CCCCCCCCCCCC
Similarity: 0.676
Experimental value : NON-Carcinogen
Predicted value : Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

✗	Global AD Index AD index = 0 Explanation: The predicted compound is outside the Applicability Domain of the model.
⚠	Similar molecules with known experimental value Similarity index = 0.733 Explanation: Only moderately similar compounds with known experimental value in the training set have been found..
✗	Accuracy of prediction for similar molecules Accuracy index = 0 Explanation: Accuracy of prediction for similar molecules found in the training set is not adequate..
✗	Concordance for similar molecules Concordance index = 0.498 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value..
✓	Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
✓	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..
✓	Model class assignment reliability Pos/Non-Pos difference = 0.595 Explanation: model class assignment is well defined..
✗	Neural map neurons concordance Neurons concordance = 0.5 Explanation: predicted substance falls into a neuron that is populated by no compounds of the training set..

Symbols explanation:

✓ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✗ The feature has a bad assessment, model is not reliable regarding this aspect.

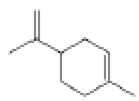
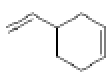
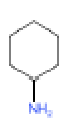
1. Prediction Summary

Prediction for compound Molecule 0 -

	Prediction: Reliability: Prediction is NON-Carcinogen, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues: - Only moderately similar compounds with known experimental value in the training set have been found - Accuracy of prediction for similar molecules found in the training set is not adequate - similar molecules found in the training set have experimental values that disagree with the predicted value

Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Carcinogen activity: NON-Carcinogen
Structural Alerts: -
Reliability: The predicted compound is outside the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

	Compound #1 CAS: 5989-27-5 Dataset id:267 (Training Set) SMILES: C=C(C)C1CC=C(C)CC1 Similarity: 0.731 Experimental value : Carcinogen Predicted value : NON-Carcinogen
	Compound #2 CAS: 1643-20-5 Dataset id:879 (Training Set) SMILES: [O-][N+](C)(C)CCCCCCCCCCCC Similarity: 0.676 Experimental value : NON-Carcinogen Predicted value : NON-Carcinogen
	Compound #3 CAS: 100-40-3 Dataset id:238 (Training Set) SMILES: C=CC1CC=CCC1 Similarity: 0.671 Experimental value : Carcinogen Predicted value : NON-Carcinogen
	Compound #4 CAS: 75881-22-0 Dataset id:762 (Training Set) SMILES: O=NN(C)CCCCCCCCCC Similarity: 0.656 Experimental value : Carcinogen Predicted value : Carcinogen Alerts (not found also in the target): SA21 Alkyl and aryl N-nitroso groups
	Compound #5 CAS: 68107-26-6 Dataset id:527 (Training Set) SMILES: O=NN(C)CCCCCCCCCCC Similarity: 0.649 Experimental value : Carcinogen Predicted value : Carcinogen Alerts (not found also in the target): SA21 Alkyl and aryl N-nitroso groups
	Compound #6 CAS: 108-91-8 Dataset id:834 (Training Set) SMILES: NC1CCCCC1 Similarity: 0.646 Experimental value : NON-Carcinogen Predicted value : NON-Carcinogen

3.2 Applicability Domain:

Measured Applicability Domain Scores

✗	Global AD Index AD index = 0.574 Explanation: The predicted compound is outside the Applicability Domain of the model.
⚠	Similar molecules with known experimental value Similarity index = 0.701 Explanation: Only moderately similar compounds with known experimental value in the training set have been found..
✗	Accuracy of prediction for similar molecules Accuracy index = 0.47 Explanation: Accuracy of prediction for similar molecules found in the training set is not adequate..
✗	Concordance for similar molecules Concordance index = 0.47 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value..
✓	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

✓ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✗ The feature has a bad assessment, model is not reliable regarding this aspect.

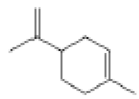
1. Prediction Summary

Prediction for compound Molecule 0 -

	Prediction: Reliability: Prediction is Possible NON-Carcinogen, but the result shows some critical aspects, which require to be checked: - Only moderately similar compounds with known experimental value in the training set have been found - some similar molecules found in the training set have experimental values that disagree with the predicted value

Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Carcinogenic activity: Possible NON-Carcinogen
No. alerts for carcinogenicity: 0
Structural Alerts: -
Reliability: The predicted compound could be out of the Applicability Domain of the model
Remarks:
none

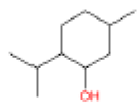
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 5989-27-5
Dataset id:218 (Training Set)
SMILES: C=C(C)C1CC=C(C)CC1
Similarity: 0.731
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 39

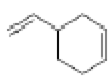


Compound #2

CAS: 15356-70-4
Dataset id:654 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.713
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #3

CAS: 1643-20-5
Dataset id:777 (Training Set)
SMILES: [O-][N+](C)(C)CCCCCCCCCCCC
Similarity: 0.676
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #4

CAS: 100-40-3
Dataset id:196 (Training Set)
SMILES: C=CC1CC=CCC1
Similarity: 0.671
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 39

Compound #5

CAS: 75881-22-0
Dataset id:595 (Training Set)
SMILES: O=NN(C)CCCCCCCCCC
Similarity: 0.656
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 1; Carcinogenity alert no. 14; Carcinogenity alert no. 27

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

Compound #6

CAS: 68107-26-6
Dataset id:439 (Training Set)
SMILES: O=NN(C)CCCCCCCCCCC
Similarity: 0.649
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 1; Carcinogenity alert no. 14; Carcinogenity alert no. 27

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.753
Explanation: The predicted compound could be out of the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.705
Explanation: Only moderately similar compounds with known experimental value in the training set have been found..

Accuracy of prediction for similar molecules
Accuracy index = 1
Explanation: Accuracy of prediction for similar molecules found in the training set is good..

Concordance for similar molecules
Concordance index = 0.649
Explanation: some similar molecules found in the training set have experimental values that disagree with the predicted value..

Atom Centered Fragments similarity check
ACF index = 1
Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.

The feature has a non optimal assessment, this aspect should be reviewed by an expert.

The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

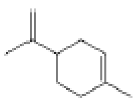
	Prediction: Reliability: Prediction is Possible NON-Carcinogen, but the result shows some critical aspects, which require to be checked: - Only moderately similar compounds with known experimental value in the training set have been found - Accuracy of prediction for similar molecules found in the training set is not optimal - some similar molecules found in the training set have experimental values that disagree with the predicted value

Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Carcinogenic activity: Possible NON-Carcinogen
No. alerts for carcinogenicity: 0
Structural Alerts: -
Reliability: The predicted compound could be out of the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

Compound #1

CAS: 104-76-7
Dataset id:314 (Training Set)
SMILES: OCC(CC)CCCC
Similarity: 0.736
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen

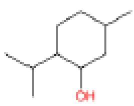


Compound #2

CAS: 5989-27-5
Dataset id:412 (Training Set)
SMILES: C=C(C)C1CC=C(C)CC1
Similarity: 0.731
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #3

CAS: 111-68-2
Dataset id:357 (Test Set)
SMILES: NCCCCCCC
Similarity: 0.713
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #4

CAS: 89-78-1
Dataset id:427 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.713
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #5

CAS: 35449-36-6
Dataset id:345 (Training Set)
SMILES: OCC(C)(C)CCCCCCC(C)(C)CO
Similarity: 0.695
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #6

CAS: 1643-20-5
Dataset id:273 (Training Set)
SMILES: [O-][N+](C)(C)CCCCCCCCCCCC
Similarity: 0.676
Experimental value : NON-Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 64

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index AD index = 0.694 Explanation: The predicted compound could be out of the Applicability Domain of the model.

Similar molecules with known experimental value Similarity index = 0.726 Explanation: Only moderately similar compounds with known experimental value in the training set have been found..
Accuracy of prediction for similar molecules Accuracy index = 0.664 Explanation: Accuracy of prediction for similar molecules found in the training set is not optimal..
Concordance for similar molecules Concordance index = 0.664 Explanation: some similar molecules found in the training set have experimental values that disagree with the predicted value..
Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.

The feature has a non optimal assessment, this aspect should be reviewed by an expert.

The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

	Prediction: ● Reliability: ★★★ **Prediction is NON-Carcinogen, the result appears reliable. Anyhow, you should check it through the evaluation of the information given in the following sections.**

Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Oral Carcinogenic class: NON-Carcinogen
Reliability: The predicted compound is into the Applicability Domain of the model
Remarks:
none

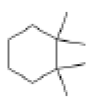
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

Compound #1

CAS: 124-18-5
Dataset id:425 (Training Set)
SMILES: CCCCCCCCCC
Similarity: 0.964
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #2

CAS: 111-84-2
Dataset id:610 (Training Set)
SMILES: CCCCCCCCC
Similarity: 0.943
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

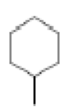


Compound #3

CAS: 30501-43-0
Dataset id:692 (Training Set)
SMILES: CC1(C)(CCCCC1(C)(C))
Similarity: 0.847
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #4

CAS: 110-54-3
Dataset id:540 (Training Set)
SMILES: CCCCCC
Similarity: 0.83
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #5

CAS: 108-87-2
Dataset id:587 (Training Set)
SMILES: CC1CCCCC1
Similarity: 0.813
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #6

CAS: 109-66-0
Dataset id:626 (Training Set)
SMILES: CCCCC
Similarity: 0.782
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

3.2 Applicability Domain:

Measured Applicability Domain Scores

Global AD Index AD index = 0.976 Explanation: The predicted compound is into the Applicability Domain of the model.
Similar molecules with known experimental value Similarity index = 0.953 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
Accuracy of prediction for similar molecules Accuracy index = 1 Explanation: Accuracy of prediction for similar molecules found in the training set is good..
Concordance for similar molecules Concordance index = 1 Explanation: Similar molecules found in the training set have experimental values that agree with the predicted value..
Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

The feature has a good assessment, model is reliable regarding this aspect.

The feature has a non optimal assessment, this aspect should be reviewed by an expert.

The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

	Prediction: ● Reliability: ★★★ **Prediction is NON-Carcinogen, the result appears reliable. Anyhow, you should check it through the evaluation of the information given in the following sections.**

Compound: Molecule 0
Compound SMILES: CCCCCCCCCC(C)C
Experimental value: -
Predicted Inhalation Carcinogenic class: NON-Carcinogen
Reliability: The predicted compound is into the Applicability Domain of the model
Remarks:
none

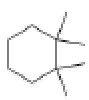
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

Compound #1

CAS: 124-18-5
Dataset id:389 (Training Set)
SMILES: CCCCCCCCCC
Similarity: 0.964
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #2

CAS: 111-84-2
Dataset id:593 (Training Set)
SMILES: CCCCCCCCC
Similarity: 0.943
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

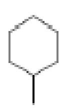


Compound #3

CAS: 30501-43-0
Dataset id:687 (Training Set)
SMILES: CC1(C)(CCCCC1(C)(C))
Similarity: 0.847
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #4

CAS: 110-54-3
Dataset id:516 (Training Set)
SMILES: CCCCCC
Similarity: 0.83
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #5

CAS: 108-87-2
Dataset id:567 (Training Set)
SMILES: CC1CCCCC1
Similarity: 0.813
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #6

CAS: 109-66-0
Dataset id:612 (Training Set)
SMILES: CCCCC
Similarity: 0.782
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

3.2 Applicability Domain:

Measured Applicability Domain Scores

✔	Global AD Index AD index = 0.976 Explanation: The predicted compound is into the Applicability Domain of the model.
✔	Similar molecules with known experimental value Similarity index = 0.953 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✔	Accuracy of prediction for similar molecules Accuracy index = 1 Explanation: Accuracy of prediction for similar molecules found in the training set is good..
✔	Concordance for similar molecules Concordance index = 1 Explanation: Similar molecules found in the training set have experimental values that agree with the predicted value..
✔	Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
✔	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

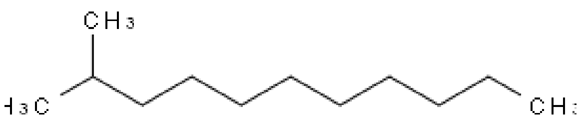
✔ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✖ The feature has a bad assessment, model is not reliable regarding this aspect.

APPENDIX F: Danish QSAR Carcinogenicity Results for Isododecane (CAS #31807-55-3)

Structure (as used for QSAR prediction):



SMILES (used for QSAR prediction): C(C)(C)CCCCCCCCC

ID

Registry Number	31807-55-3	PubChem CID	
REACH EC Number (pre-registration, by 2013)	250-816-8	REACH EC Number (registration, 2019 or 2022)	
REACH registration (2022)		REACH registration cumulated minimum annual tonnage (2022)	
EU CLP Harmonized Classification*		DK-EPA / DTU QSAR-based CLP Advisory Classification	Acute Tox. 4
EU Biocide active substances		EU Pesticide active substances	
EU EFSA Botanical substances		US TSCA (Oct. 2021)	Yes
Tox21 (2019)		ToxCast (Oct. 2021)	
Molecular Formula	C12 H26	Molecular weight (g/mole)	170.34
Chemical Name	isododecane		

(Annex VI to CLP up to and including the 9th ATP, and including Nordic Council of Minister SPIN list for group entries)

Carcinogenicity

	E Ultra	Leadscope
FDA RCA Cancer Male Rat	NEG_IN	INC_OUT
FDA RCA Cancer Female Rat	NEG_IN	INC_OUT
FDA RCA Cancer Rat	NEG_IN	INC_OUT
FDA RCA Cancer Male Mouse	NEG_IN	INC_OUT
FDA RCA Cancer Female Mouse	NEG_IN	INC_OUT
FDA RCA Cancer Mouse	NEG_IN	NEG_OUT
FDA RCA Cancer Rodent	NEG_IN	INC_OUT

Commercial models from CASE Ultra and Leadscope

FDA RCA: Data from US Food and Drug Administration as part of Research Cooperation Agreement

Carcinogenicity (genotox and nongenotox) alerts by ISS, alerts in:	
- parent only	No alert found
Oncologic Primary Classification, alerts in:	
- parent only	Not classified

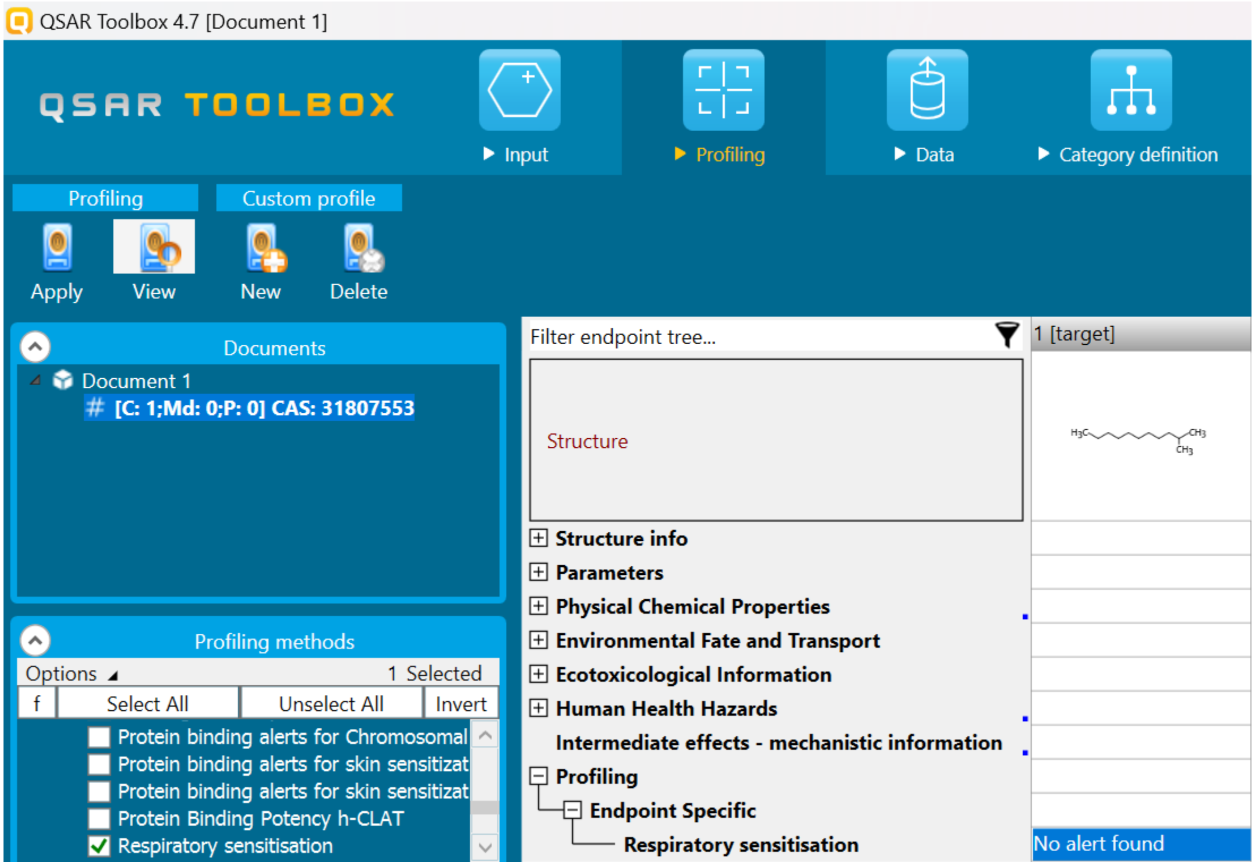
OECD QSAR Toolbox v.4.2 profilers

Profiler predictions are supporting information to be used together with the relevant QSAR predictions

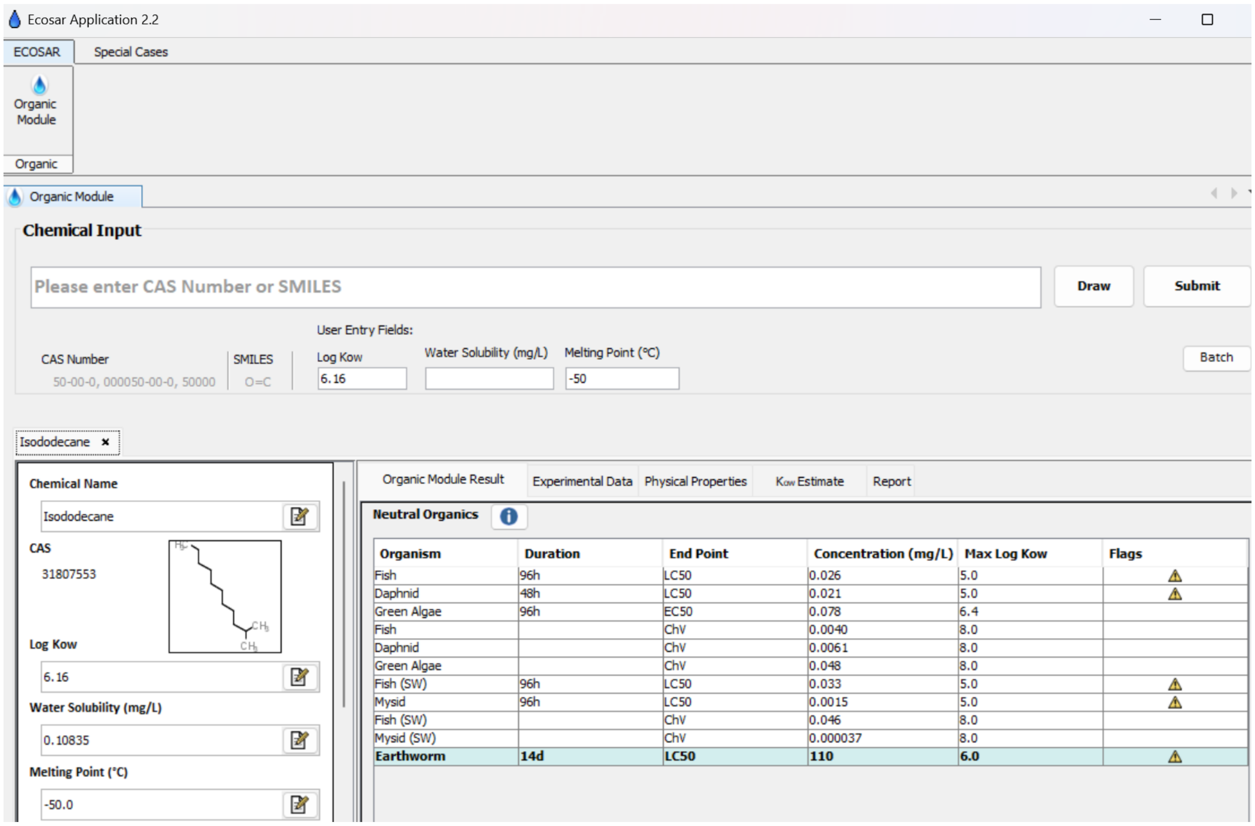
	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Liver Specific Cancer in Rat or Mouse		NEG_OUT	NEG_IN	NEG_OUT	INC_OUT

DTU-developed models

APPENDIX G: OECD QSAR Toolbox Respiratory Sensitization Results for Isododecane (CAS #31807-55-3)



APPENDIX H: ECOSAR Modeling Results for Isododecane (CAS #31807-55-3)



Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Fish	96h	LC50	0.026	5.0	⚠
Daphnid	48h	LC50	0.021	5.0	⚠
Green Algae	96h	EC50	0.078	6.4	
Fish		ChV	0.0040	8.0	
Daphnid		ChV	0.0061	8.0	
Green Algae		ChV	0.048	8.0	
Fish (SW)	96h	LC50	0.033	5.0	⚠
Mysid	96h	LC50	0.0015	5.0	⚠
Fish (SW)		ChV	0.046	8.0	
Mysid (SW)		ChV	0.000037	8.0	
Earthworm	**14d**	**LC50**	**110**	**6.0**	⚠

APPENDIX I: EPI Suite™ Modeling Results for Isododecane (CAS #31807-55-3)

(Estimated values included in the GreenScreen® are highlighted and bolded)

```
CAS Number: 31807-55-3
SMILES : CC(CCCCCCCCC)C
CHEM   : Isododecane
MOL FOR: C12 H26
MOL WT : 170.34
------------------------------ EPI SUMMARY (v4.11) --------------------------
 Physical Property Inputs:
    Log Kow (octanol-water):   ------
    Boiling Point (deg C)  :   178.00
    Melting Point (deg C)  :   -50.00
    Vapor Pressure (mm Hg) :   ------
    Water Solubility (mg/L):   ------
    Henry LC (atm-m3/mole) :   ------

 Log Octanol-Water Partition Coef (SRC):
    Log Kow (KOWWIN v1.69 estimate) =  6.16

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
    Boiling Pt (deg C):  193.70  (Adapted Stein & Brown method)
    Melting Pt (deg C):  -31.86  (Mean or Weighted MP)
    VP(mm Hg,25 deg C):  1.45  (Mean VP of Antoine & Grain methods)
    VP (Pa, 25 deg C) :  193  (Mean VP of Antoine & Grain methods)

 Water Solubility Estimate from Log Kow (WSKOW v1.42):
    Water Solubility at 25 deg C (mg/L):  0.1081
       log Kow used: 6.16 (estimated)
       melt pt used: -50.00 deg C

 Water Sol Estimate from Fragments:
    Wat Sol (v1.01 est) =  0.015515 mg/L

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

 Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
   Bond Method :   9.35E+000  atm-m3/mole  (9.47E+005 Pa-m3/mole)
   Group Method:   1.62E+001  atm-m3/mole  (1.64E+006 Pa-m3/mole)
 For Henry LC Comparison Purposes:
   User-Entered Henry LC:  not entered
   Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
      HLC:  3.006E+000 atm-m3/mole  (3.046E+005 Pa-m3/mole)
      VP:   1.45 mm Hg (source: MPBPVP)
      WS:   0.108 mg/L (source: WSKOWWIN)
```

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: 6.16 (KowWin est)
Log Kaw used: 2.582 (HenryWin est)
Log Koa (KOAWIN v1.10 estimate): 3.578
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 0.7749
Biowin2 (Non-Linear Model) : 0.9194
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.1211 (weeks)
Biowin4 (Primary Survey Model) : 3.8710 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.5449
Biowin6 (MITI Non-Linear Model): 0.7309
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.3217
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
LOG BioHC Half-Life (days) : 1.0213
BioHC Half-Life (days) : 10.5030

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 176 Pa (1.32 mm Hg)
Log Koa (Koawin est): 3.578
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 1.7E-008
Octanol/air (Koa) model: 9.29E-010
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 6.16E-007
Mackay model : 1.36E-006
Octanol/air (Koa) model: 7.43E-008

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 13.9282 E-12 cm3/molecule-sec
Half-Life = 0.768 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 9.215 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
9.9E-007 (Junge-Pankow, Mackay avg)
7.43E-008 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 4053 L/kg (MCI method)
Log Koc: 3.608 (MCI method)

Koc : 2.218E+005 L/kg (Kow method)
Log Koc: 5.346 (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 = 2.358 (BCF = 227.9 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 0.6914 days (HL = 4.913 days)
Log BCF Arnot-Gobas method (upper trophic) = 3.310 (BCF = 2043)
Log BAF Arnot-Gobas method (upper trophic) = 3.897 (BAF = 7892)
log Kow used: 6.16 (estimated)

Volatilization from Water:
Henry LC: 9.35 atm-m3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 1.332 hours
Half-Life from Model Lake : 124 hours (5.165 days)

Removal In Wastewater Treatment (recommended maximum 95%):
Total removal: 99.94 percent
Total biodegradation: 0.18 percent
Total sludge adsorption: 59.15 percent
Total to Air: 40.61 percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)

	Mass Amount (percent)	**Half-Life (hr)**	**Emissions (kg/hr)**
Air	**19.1**	**18.4**	**1000**
Water	**70.9**	**360**	**1000**
Soil	**1.7**	**720**	**1000**
Sediment	**8.33**	**3.24e+003**	**0**

Persistence Time: 89.3 hr

Level III Fugacity Model: (MCI Method with Water percents)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	19.1	18.4	1000
Water	70.9	360	1000
water	(65.7)		
biota	(4.75)		
suspended sediment	(0.399)		
Soil	1.7	720	1000
Sediment	8.33	3.24e+003	0

Persistence Time: 89.3 hr

Level III Fugacity Model: (EQC Default)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)

```
Air       2.15          18.4        1000
Water     8.39          360         1000
  water     (4.28)
  biota     (0.309)
  suspended sediment (3.8)
Soil      14.5          720         1000
Sediment  74.9          3.24e+003   0
  Persistence Time: 632 hr
```

APPENDIX J: 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

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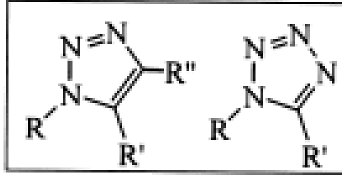
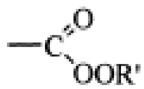
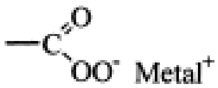
Explosivity – Full List

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
>CN_2	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
>C=N−O—Metal	Metal Fulminates or *aci*-Nitro Salts
>N−Metal	N-Metal Derivatives (especially heavy metals)
>N−N=O >N−NO_2	N-Nitroso and N-Nitro Compounds
>N^+−N−NO_2	N-Azolium Nitroimidates
>C−N=N−C<	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

Screening procedures

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

Structural feature	Chemical classes
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidising agents
S=O	Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides
P–O	Phosphites
Strained rings	Epoxides, aziridines
Unsaturation	Olefins, cyanates

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APPENDIX K: Change in Benchmark Score

Table 6 provides a summary of changes to the GreenScreen® Benchmark™ for isododecane. This is a new GreenScreen® assessment.

Table 6: Change in GreenScreen® Benchmark™ for Isododecane

Date	**GreenScreen® Benchmark™**	**GreenScreen® Version**	**Comment**
December 27, 2024	BM-2	v. 1.4	Original GreenScreen® assessment.

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