Trimethylbenzenes (CAS #95-63-6, 108-67-8, 526-73-6, 25551-13-7) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

Washington State Department of Ecology

Prepared by:

ToxServices LLC

October 15, 2014

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

TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Trimethylbenzenes (CAS #95-63-6, 108-67-8, 526-73-6, 25551-13-7)

Trimethylbenzenes are chemicals that function as solvents and intermediates in the production of dyes, perfumes, and resins, as paint thinners, as motor fuel components, and as a co-monomer in the production of pseudocumene-formaldehyde resins (1,2,4-trimethylbenzene only).

Trimethylbenzenes were assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as they have Moderate Group I Human Health Hazard (mutagenicity/genotoxicity (M) and reproductive toxicity (R)), High persistence (P), Very High Group II Human Health Toxicity (single dose neurotoxicity (Ns)), High Group II* Human Toxicity (repeated dose neurotoxicity (Nr*)), and High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA)). This corresponds to GreenScreen® benchmark classifications 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)"), 2e ("Moderate T (Group I Human)"), and 2f ("Very High T (Ecotoxicity or Group II Human) or High T (Group II* Human)") in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Conduct a Data Gap Analysis to assign a final Benchmark score), trimethylbenzenes meet requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if trimethylbenzenes were assigned a High score for the data gap endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

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

GreenScreen® Hazard Ratings for Trimethylbenzenes

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

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

GreenScreen® Assessment for Trimethylbenzenes (CAS #95-63-6)

Method Version: GreenScreen® Version 1.2[1]
Assessment Type[2]: Certified

Chemical Name: Trimethylbenzenes

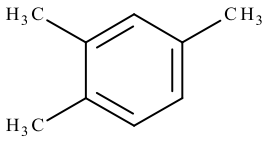
CAS Number: 95-63-6, 108-67-8, 526-73-8, 25551-13-7

GreenScreen® Assessment Prepared By:
Name: Zach Guerrette, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: September 23, 2014
Assessor Type: Licensed GreenScreen® Profiler

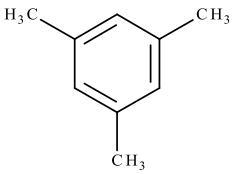
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: October 15, 2014

Confirm application of the *de minimus* rule[3]: N/A

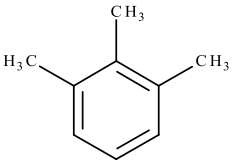
Chemical Structure(s):



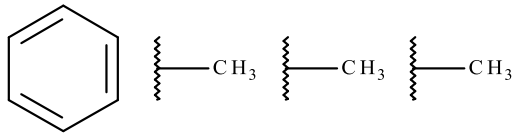
1,2,4-Trimethylbenzene
(CAS #95-63-6)



1,3,5-Trimethylbenzene
(CAS #108-67-8)



1,2,3-Trimethylbenzene
(CAS #526-73-8)



Trimethylbenzenes
(CAS #25551-13-7)

Also called:
1,2,4-Trimethylbenzene (CAS #95-63-6)
Pseudocumene; 1,2,5-Trimethylbenzene; 1,3,4-Trimethylbenzene; as-Trimethylbenzene; Asymmetrical trimethylbenzene; Benzene, 1,2,4-trimethyl-; Benzene, 1,2,5-trimethyl-; EINECS 202-436-9;

[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2

[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen® Verification Program)

[3] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

Pseudocumol; psi-Cumene; Psi-cumene; Uns-trimethylbenzene; 1,2,4-Trimethyl benzene (ChemIDplus 2014a)

1,3,5-Trimethylbenzene (CAS #108-67-8)
Mesitylene; 3,5-Dimethyltoluene; Benzene, 1,3,5-trimethyl-; EINECS 203-604-4; sym-Trimethylbenzene; Trimethylbenzol; 1,3,5-Trimethylbenzene [UN2325] [Flammable liquid]; Trimethylbenzene, 1,3,5-; UN2325 (ChemIDplus 2014b)

1,2,3-Trimethylbenzene (CAS #526-73-8)
Hemimellitene; EINECS 208-394-8; Hemellitol; Hemimellitol; Benzene, 1,2,3-trimethyl- (ChemIDplus 2014c)

Trimethylbenzenes (CAS #25551-13-7)
EINECS 247-099-9; Methylxylene; Trimethyl benzene; Trimethylbenzene; Benzene, trimethyl-; Benzene, trimethyl- (mixed isomers); Trimethyl benzene (mixed isomers) (ChemIDplus 2014d)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
For some endpoints, reproductive toxicity, skin sensitization, and eye irritation, no data were identified for the trimethylbenzenes. Data for aromatic naphtha, type 1 (CAS #64742-95-6), which is a complex combination of hydrocarbons obtained from distillation of aromatic streams and consists predominantly of aromatic hydrocarbons having carbon numbers mostly in the range of C8-C10 (ChemIDplus 2014e), which include the trimethylbenzenes, were used for the reproductive toxicity, skin sensitization, and eye irritation endpoints in the REACH dossiers for 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene. ToxServices used data for aromatic naphtha, type 1 (CAS #64742-95-6) to address the data gaps for trimethylbenzenes.

No chemical structure is available for aromatic naphtha, type 1 (CAS #64742-95-6) as it is a complex mixture.

Identify Applications/Functional Uses (HSDB 2008a,b,c)**:**
1. Solvent and intermediate in the production of dyes, perfumes, and resins.
2. Paint thinner.
3. Motor fuel component.
4. Co-monomer in the production of pseudocumene-formaldehyde resins (1,2,4-trimethylbenzene only).

GreenScreen® Summary Rating for Trimethylbenzenes[4]: Trimethylbenzenes were assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as they have Moderate Group I Human Health Hazard (mutagenicity/genotoxicity (M) and reproductive toxicity (R)), High persistence (P), Very High Group II Human Health Toxicity (single dose neurotoxicity (Ns)), High Group II* Human Toxicity (repeated dose neurotoxicity (Nr*)), and High Ecotoxicity (acute aquatic toxicity (AA) and chronic aquatic toxicity (CA)). This corresponds to GreenScreen® benchmark classifications 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)"), 2e ("Moderate T (Group I Human)"), and 2f ("Very High T (Ecotoxicity or Group II Human) or High T (Group II* Human)") in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Conduct a Data Gap Analysis to assign a final

[4] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

Benchmark score), trimethylbenzenes meet requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if trimethylbenzenes were assigned a High score for the data gap endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Trimethylbenzenes

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

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

Transformation Products and Ratings:

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[5]

No information on transformation products was identified for trimethylbenzenes. 1,2,4-Trimethylbenzene, 1,3,5-trimethylbenzene, and 1,2,3-trimethylbenzene are not expected to undergo hydrolysis based on the lack of hydrolysable functional groups (HSDB 2008a,b,c). Therefore, the Benchmark Score for trimethylbenzenes is not adjusted by transformation products.

Introduction

1,2,4-Trimethylbenzene is used as a solvent in the production of dyes, perfumes, and resins, is a co-monomer for pseudocumene-formaldehyde resins, and is used as a paint thinner (HSDB 2008a). It is produced via fractional distillation of the C9 fraction of refinery reformate streams, via the liquid-phase disproportionation of xylene in the presence of aluminum chloride, or via the methylation of xylene with methanol or dimethyl ether on fluorine-containing crystalline borosilicate, aluminosilicate, or boroaluminosilicate at 300°C and atmospheric pressure (HSDB 2008a).

1,3,5-Trimethylbenzene is used as a solvent, paint thinner, motor fuel component, and intermediate for the production of dyes and antioxidants (HSDB 2008b). It is produced via the dehydration of acetone with sulfuric acid or via the liquid-phase disproportionation of xylene in the presence of aluminum chloride (HSDB 2008b).

1,2,3-Trimethylbenzene is used as a solvent in dye and perfume production (HSDB 2008c). It is produced via the distillation and purified by the differential hydrolysis of its sulfonic acids (HSDB 2008c).

ToxServices assessed trimethylbenzenes against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.69 (GreenScreen® Hazard Assessment) (ToxServices 2013).

[5] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b) and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for trimethylbenzenes can be found in Appendix C and a summary of the results can be found below:

1,2,4-Trimethylbenzene, CAS #95-63-6

- High Hazard:
  - Eye Irritation
    - GHS Hazard Statement H319 – causes serious eye irritation
  - Skin Irritation
    - GHS Hazard Statement H315 – causes skin irritation
    - EU Risk Phrase R36/37/38 – irritating to eyes, respiratory system and skin
  - Acute Aquatic Toxicity
    - EU Risk Phrase R51/53 – toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
    - GHS Japan Category 2 – hazardous to the aquatic environment
  - Chronic Aquatic Toxicity
    - GHS Hazard Phrase H411 – toxic to aquatic life with long-lasting effects
    - GHS Japan Category 2 – hazardous to the aquatic environment
- Medium Hazard:
  - Eye Irritation
    - EU Risk Phrase R36/37/38 – irritating to eyes, respiratory system and skin
    - GHS New Zealand Category 6.4A (equivalent to GHS Category 2 eye irritant) – irritating to the eye
  - Skin Irritation
    - GHS New Zealand Category 6.3B (equivalent to GHS Category 3 skin irritant) – mildly irritating to the skin
  - Chronic Aquatic Toxicity
    - GHS New Zealand Category 9.1B (fish, crustacean) (equivalent to GHS Category 2 chronic aquatic toxicant) – very ecotoxic in the aquatic environment
  - Developmental Toxicity
    - German MAK Pregnancy Group C
  - Acute Toxicity
    - GHS Hazard Statement H332 – harmful if inhaled
    - EU Risk Phrase R20 – harmful by inhalation
    - GHS New Zealand Category 6.1D (inhalation) (equivalent to GHS Category 4 inhalation toxicant) – acutely toxic
  - Systemic Toxicity (single dose)
    - GHS Japan Category 3 specific target organs/systemic toxicity following single exposure
    - GHS Hazard Statement H335 – may cause respiratory irritation
    - EU Risk Phrase R36/37/38 – irritating to eyes, respiratory system and skin
  - Systemic Toxicity (repeat dose)

        - GHS Japan Category 2 specific target organs/systemic toxicity following repeated exposure
        - GHS New Zealand Category 6.9B (inhalation) (equivalent to GHS Category 2 specific target organ systemic toxicant) – harmful to human target organs or systems
    - Flammability
        - GHS Hazard Statement H226 – flammable liquid and vapor
        - EU Risk Phrase R10 – flammable liquid
        - Quebec CSST WHMIS classifications Class B3 – combustible liquids
        - GHS New Zealand Category 3.1C (equivalent to GHS Category 3) – flammable liquids: medium hazard
        - GHS Japan Category 3 flammable liquid
- 1,2,4-Trimethylbenzene is not listed on the U.S. DOT (2008a,b) lists.

<u>1,3,5-Trimethylbenzene, CAS #108-67-8</u>

- High Hazard:
    - Acute Aquatic Toxicity
        - EU Risk Phrase R51/53 – toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
        - GHS Japan Category 2 – hazardous to the aquatic environment (acute)
    - Chronic Aquatic Toxicity
        - GHS Hazard Statement H411 – toxic to aquatic life with long-lasting effects
        - GHS Japan Category 2 – hazardous to the aquatic environment (chronic)
        - GHS New Zealand Category 9.1B (crustacean) (equivalent to GHS Category 2 chronic aquatic toxicant) – very ecotoxic in the aquatic environment
        - GHS New Zealand Category 9.1C (fish, algae) (equivalent to GHS Category 3 chronic aquatic toxicant) – harmful in the aquatic environment
- Medium Hazard:
    - Developmental Toxicity
        - German MAK Pregnancy Risk Group C
    - Systemic Toxicity (single dose)
        - GHS Hazard Statement H335 – may cause respiratory irritation
        - EU Risk Phrase R37 – irritating to the respiratory system
        - GHS Japan Category 3 specific target organs/systemic toxicity following single exposure
    - Eye Irritation
        - GHS Japan Category 2B – serious eye damage/eye irritation
        - GHS New Zealand Category 6.4A (equivalent to GHS Category 2 eye irritant) – irritating to the eye
    - Skin irritation
        - GHS Japan Category 2 skin irritant
        - GHS New Zealand Category 6.3B (equivalent to GHS Category 3 skin irritant) – mildly irritating to the skin.
    - Flammability
        - GHS Hazard Statement H226 – flammable liquid and vapor
        - EU Risk Phrase R10 – flammable liquid
        - Quebec CSST WHMIS classification Class B3 – combustible liquids
        - GHS Japan Category 3 flammable liquid

        - GHS New Zealand Category 3.1C (equivalent to GHS Category 3 flammable liquid) flammable liquid: medium hazard
- 1,3,5-Trimethylbenzene is listed in U.S. DOT (2008a) as a hazard class 3, PG III (minor danger), label code 3 (flammable liquid) chemical. It is not listed in U.S. DOT (2008b).

1,2,3-Trimethylbenzene, CAS #526-73-8

- Medium Hazard:
    - Developmental Toxicity
        - German MAK Pregnancy Risk Group C
    - Flammability
        - Quebec CSST WHMIS Class B3 – combustible liquids
        - GHS New Zealand Category 3.1C (equivalent to GHS Category 3 flammable liquid) flammable liquid: medium hazard
- 1,2,3-Trimethylbenzene is not listed on the U.S. DOT (2008a,b) lists.

Trimethylbenzenes, CAS #25551-13-7

- Trimethylbenzenes are not listed in Pharos.
- 1,2,3-Trimethylbenzene is not listed on the U.S. DOT (2008a,b) lists.

Physicochemical Properties of Trimethylbenzenes

1,2,4-Trimethylbenzene is a clear, colorless liquid under standard temperature and pressure. It has a vapor pressure of 2.1-2.25 mm Hg indicating that it will exist mostly in the vapor (gas) phase. It is slightly soluble in water (57 mg/L) and is more soluble in octanol than water (log K_{ow} = ~3.6). The log K_{ow} of less than 4 indicates that it has low potential to bioaccumulate in aquatic biota.

Table 1: Physical and Chemical Properties of 1,2,4-Trimethylbenzene (CAS #95-63-6)

Property	Value	Reference
Molecular formula	C_9H_{12}	ChemIDplus 2014a
SMILES Notation	c1(c(ccc(c1)C)C)C	ChemIDplus 2014a
Molecular weight	120.194 g/mol	ChemIDplus 2014a
Physical state	Liquid	ECHA 2014a
Appearance	Clear, colorless	ECHA 2014a
Melting point	-43.8°C -43.77°C	ChemIDplus 2014a ECHA 2014a
Vapor pressure	2.1 mm Hg at 25°C 0.3 kPa (2.25 mm Hg) at 25°C	ChemIDplus 2014a ECHA 2014a
Water solubility	57 mg/L at 25°C	ECHA 2014a
Dissociation constant	Not identified	
Density/specific gravity	0.88 g/cm^3 at 20°C	ECHA 2014a
Partition coefficient	Log K_{ow} = 3.63 Low K_{ow} = 3.65	ChemIDplus 2014a ECHA 2014a

1,3,5-Trimethylbenzene is a clear, colorless liquid under standard temperature and pressure. It has a vapor pressure of ~2.4 mm Hg indicating that it will exist mostly in the vapor (gas) phase. It is slightly soluble in water (48.2 mg/L) and is more soluble in octanol than water (log K_{ow} = 3.42-3.84). The log K_{ow} of less than 4 indicates that it has low potential to bioaccumulate in aquatic biota.

Table 2: Physical and Chemical Properties of 1,3,4-Trimethylbenzene (CAS #108-67-8)		
Property	**Value**	**Reference**
Molecular formula	C_9H_{12}	ChemIDplus 2014b
SMILES Notation	c1(cc(cc(c1)C)C)C	ChemIDplus 2014b
Molecular weight	120.194 g/mol	ChemIDplus 2014b
Physical state	Liquid	ECHA 2014b
Appearance	Clear, colorless	ECHA 2014b
Melting point	-44.7°C -44.72°C	ChemIDplus 2014b ECHA 2014b
Vapor pressure	2.48 mm Hg at 25°C 3.2 hPa (2.4 mm Hg) at 25°C	ChemIDplus 2014b ECHA 2014b
Water solubility	48.2 mg/L at 25C 48.2 mg/L at 25°C	ChemIDplus 2014b ECHA 2014b
Dissociation constant	Not identified	
Density/specific gravity	0.86 g/cm^3 at 25°C	ECHA 2014b
Partition coefficient	Log K_{ow} = 3.42 Low K_{ow} = 3.42-3.84	ChemIDplus 2014b ECHA 2014b

1,2,3-Trimethylbenzene is a clear, colorless liquid under standard temperature and pressure. It has a vapor pressure of 1.69 mm Hg indicating that it will exist mostly in the vapor (gas) phase. It is slightly soluble in water (75.2 mg/L) and is more soluble in octanol than water (log K_{ow} = 3.66). The log K_{ow} of less than 4 indicates that it has low potential to bioaccumulate in aquatic biota.

Table 3: Physical and Chemical Properties of 1,2,3-Trimethylbenzene (CAS #526-73-8)		
Property	**Value**	**Reference**
Molecular formula	C_9H_{12}	ChemIDplus 2014c
SMILES Notation	c1(c(cccc1C)C)C	ChemIDplus 2014c
Molecular weight	120.194 g/mol	ChemIDplus 2014c
Physical state	Liquid	HSDB 2008c
Appearance	Clear, colorless	HSDB 2008c
Melting point	-25.4°C	ChemIDplus 2014c
Vapor pressure	1.69 mm Hg at 25°C	ChemIDplus 2014c
Water solubility	75.2 mg/L at 25°C	ChemIDplus 2014c
Dissociation constant	Not identified	
Density/specific gravity	0.8944 g/cm^3 at 20°C	HSDB 2008c
Partition coefficient	Log K_{ow} = 3.66	ChemIDplus 2014c

Hazard Classification Summary Section:

<u>Group I Human Health Effects (Group I Human)</u>

Carcinogenicity (C) Score (H, M, or L): *L*
Trimethylbenzenes were assigned a score of Low for carcinogenicity based on no structural alerts and no statistically significant increase in the tumor incidence in a study performed with 1,2,4-trimethylbenzene. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when

negative data, no structural alerts, and no GHS classification are available (CPA 2012a). The confidence in the score was adjusted as it is based on modeling and a low-quality animal study.

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - U.S. EPA 2013
    - Rats were exposed to 1,2,4-trimethylbenzene (purity not specified) at 0 or 800 mg/kg/day via gavage for an unspecified amount of time. A marginal increase in the total malignant tumors and head tumors, described as neuroesthesioepitheliomas, was observed. No statistical analysis was performed by the study authors. When the U.S. EPA performed a statistical analysis on the percentages of animals exhibiting tumors in the control and treatment groups, no statistically significant increase was identified with treatment.
- In the absence of quality studies, ToxServices modeled the carcinogenicity of the trimethylbenzenes using ToxTree.
  - ToxTree 2013
    - 1,2,4-Trimethylbenzene, 1,3,5-trimethylbenzene, and 1,2,3-trimethylbenzene do not have structural alerts for genotoxic or non-genotoxic carcinogenicity (see Appendix G).
- Based on the lack of structural alerts for genotoxic and non-genotoxic carcinogenicity and the lack of statistical significance in the U.S. EPA's analysis of the study performed with 1,2,4-trimethylbenzene, ToxServices concluded that trimethylbenzenes have a Low potential for carcinogenicity.

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

Trimethylbenzenes were assigned a score of Moderate for mutagenicity/genotoxicity based on positive results in bone marrow sister chromatid exchange assays performed with 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene. GreenScreen® criteria classify chemicals as a Moderate hazard for mutagenicity/genotoxicity when limited or marginal evidence of mutagenicity is observed in animals (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a
    - *In vitro*: Negative results were obtained for mutagenicity in a bacterial reverse mutation test conducted in a manner similar to OECD 471 (only 4 strains tested). *Salmonella typhimurium* tester strains TA 97a, TA 98, TA 100, and TA 102 were exposed to 1,2,4-trimethylbenzene (purity not specified) at 1-30 µg/plate, with and without metabolic activation. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.
    - *In vivo*: Negative results for clastogenicity were obtained in a mouse micronucleus test conducted in a manner similar to OECD 474 (positive control in males only).

Balb/c mice (4-23/sex/dose group) were administered two intraperitoneal injections 24 hours apart of 1,2,4-trimethylbenzene (purity not specified) at 0 (8 males and 4 females), 2,000 (12 males), 3,280 (12 females), or 4,000 (23 males) mg/kg. Bone marrow samples were collected at 30, 48, and 72 hours after the first injection. No increase in the frequency of micronuclei was observed with treatment.

- *In vivo*: Positive results for genotoxicity were obtained in an *in vivo* sister chromatid exchange assay conducted according to EPA OPPTS 870.5915. Balb/c mice (5/sex/dose group) were administered single intraperitoneal injections of 1,2,4-trimethylbenzene (purity not specified) at 900, 1,800, 2,700, or 3,600 mg/kg. The animals were sacrificed 23 hours later and bone marrow cells were isolated for evaluation of sister chromatid exchanges. An increased frequency of sister chromatid exchanges was observed with treatment, with solvent controls having incidences of 3.58-4.29, the 900 mg/kg group having an incidence of 5.46, and the 2,700 mg/kg group having an incidence of 6.61. No data were presented for the 1,800 mg/kg group. Analysis of sister chromatid exchanges in the high dose group was not possible due to 4/5 animals dying or an insufficient number of cells available for analysis.

- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014a
    - *In vitro*: Negative results were obtained for mutagenicity in a bacterial reverse mutation test conducted in a manner similar to OECD 471 (only 4 strains tested). *Salmonella typhimurium* tester strains TA 97a, TA 98, TA 100, and TA 102 were exposed to 1,3,5-trimethylbenzene (purity not specified) at 1-40 µg/plate, with and without metabolic activation. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.
    - *In vivo*: Negative results were obtained for clastogenicity in a mouse micronucleus test conducted in a manner similar to OECD 474 (positive control only in males). Balb/c mice (4-24/sex/dose group) were administered two intraperitoneal injections separated by 24 hours of 1,3,5-trimethylbenzene (purity not specified) at 0 (8 males and 4 females), 1,800 (12 males), 2,960 (12 females), or 3,600 (24 males) mg/kg. Bone marrow samples were obtained 30, 48, and 72 hours following the first injection. No increase in the frequency of micronuclei was observed with treatment.
    - *In vivo*: Positive results for genotoxicity were obtained in an *in vivo* sister chromatid exchange assay conducted according to EPA OPPTS 870.5915. Balb/c mice (5/sex/dose group) were administered single intraperitoneal injections of 1,3,5-trimethylbenzene (purity not specified) at 900, 1,800, 2,700, or 3,600 mg/kg. The animals were sacrificed 23 hours later and bone marrow cells were isolated for evaluation of sister chromatid exchanges. An increased frequency of sister chromatid exchanges was observed with treatment, with solvent controls having incidences of 3.58-4.29, the 900 mg/kg group having an incidence of 3.90, and the 2,700 mg/kg group having an incidence of 4.58. No data were presented for the 1,800 mg/kg group. Analysis of sister chromatid exchanges in the high dose group was not possible due to 2/5 animals dying or insufficient number of cells available for analysis.
- 1,2,3-Trimethylbenzene, CAS #526-73-8
  - CCRIS 2000
    - *In vitro*: Mixed results for mutagenicity were obtained in an Ames test. *S. typhimurium* tester strains TA 97A, TA 98, TA 100, and TA 102 were exposed to

1,2,3-trimethylbenzene (purity not specified) at 1-20 µL/plate, with and without metabolic activation. An increase in the mutation frequency was observed in the absence of metabolic activation, but no such increase was observed in the presence of metabolic activation. No further details provided.

- This study appears to have been conducted by the same authors as those of the Ames studies reported in ECHA. Due to lack of details on cytotoxicity and statistical analysis, this description is of limited value for this endpoint.

- Negative results for mutagenicity and clastogenicity were obtained in studies performed with 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene. Positive results were obtained from sister chromatid exchange assays performed with both of these chemicals. As mammalian bone marrow sister chromatid exchange assays are recognized as genotoxicity tests in somatic cells in the GHS criteria (see section 3.5.2.8 of UN 2013), ToxServices concluded that the positive results in the sister chromatid exchange assays are limited to marginal evidence of genotoxicity by the trimethylbenzenes in context of the negative results for mutagenicity and clastogenicity.

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

Trimethylbenzenes were assigned a score of Moderate for reproductive toxicity based on effects on male fertility, litter size, birth weight, and postnatal survival in a 2-generation study performed with the surrogate aromatic naphtha, type I. GreenScreen® criteria classify chemicals as a Moderate hazard for reproductive toxicity when limited or marginal evidence of reproductive toxicity is observed in animals (CPA 2012a). The confidence is adjusted as it is not clear if the observations were a direct effect of the treatment or an indirect effect associated with the systemic toxicity.

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- No data for the trimethylbenzenes were identified for this endpoint.
- Surrogate: Aromatic Naphtha, Type I (CAS #64742-95-6).
  - ECHA 2014a
    - A 2-generation reproduction toxicity study conducted according to an outdated version of OECD 416 was performed with Charles River COBS CD rats (30/sex/dose group) administered whole body inhalation exposures to aromatic naphtha, type I vapor at 0, 100, 500, or 1,500 ppm for 6 hours/day 5 days/week. The aromatic naphtha, type I used in the study contained 1,2,4-trimethylbenzene at 40.5%, 1,2,3-trimethylbenene at 6.18%, and 1,3,5-trimethylbenzene at 8.37% (55.05% for trimethylbenzenes in total), with the remainder made up of mostly ethyltoluenes (27.59%). The F0 males were exposed for 10 weeks prior to mating and during the 2-week mating period, and F0 females were exposed for 10 weeks prior to mating, during the 2-week mating period, during gestation until pregnancy day 20, and daily during the postnatal period from postnatal day 5 until weaning on postnatal day 21. The F1 males and females were not exposed until 5-7 weeks of age and then were exposed in the same manner as the F0 animals. The F2 males and females were exposed from postnatal day 22 in the same manner as the F0 animals. The rats were evaluated for clinical signs of toxicity, body weight, food consumption, gross pathology, histopathology, reproductive indices, the number and sex of pups, stillbirths, and live births, postnatal mortality, presence of gross abnormalities, and offspring viability indices. Mortality was observed in the high

concentration group in all generations in this study. Reproductive parameters were not affected by treatment in the first generation. In the second generation, male fertility (no details provided), litter size, birth weight, and postnatal survival were reduced in the high concentration group. These findings may be the result of several litters being exposed beyond GD 20 during pregnancy; these litters exhibited reduced number of live births, mean birth weight, and survival during the lactation period. In the third generation, 88% of the animals in the high concentration group died and there was no evidence of treatment-related effects on fertility or reproduction. The study authors identified a NOAEC of 500 ppm and concluded that there was "no consistent evidence of reproductive toxicity in the presence of systemic toxicity."

- In summary, male fertility and litter size were reduced in the high concentration group of the second generation of animals. However, significant systemic toxicity as increased mortality was observed in the high concentration group throughout the study. Therefore, ToxServices cannot determine if the reproductive effects are due to direct effects of the treatment on reproduction or are indirect effects of the systemic toxicity. Therefore, the confidence in the score for this endpoint was adjusted.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L
Trimethylbenzenes were assigned a score of Low for developmental toxicity based on the lack of developmental toxicity observed in prenatal developmental toxicity tests of 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - German MAK Pregnancy Group C (CAS #95-63-6, 108-67-8, 526-73-8)
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a
    - *Inhalation*: A prenatal developmental toxicity test conducted according to OECD 414 was performed with pregnant female Sprague-Dawley rats (17-24/dose group) administered whole body inhalation exposures to 1,2,4-trimethylbenzene vapor at 0, 492, 1,470, 2,950, or 4,430 mg/m^3 (equivalent to 0, 0.492, 1.47, 2.95, and 4.43 mg/L, respectively) for 6 hours/day on gestational days (GD) 6-20. The animals were sacrificed on GD 21. Maternal evaluations consisted of clinical signs of toxicity, body weight, food consumption, and ovarian and uterine content. Fetal examinations consisted of evaluating the incidence of external, visceral, and skeletal malformations. Decreases in maternal body weight gain were observed at 2.95 mg/L during the first half of the exposure period and throughout the exposure period at 4.43 mg/L. Food consumption significantly decreased during the exposure period at 2.95 and 4.43 mg/L. There were no treatment-related effects on the mean number of implantations and live fetuses, post-implantation loss and resorption, or on the fetal sex ratio. Fetal weights were significantly lower than control values at 295 mg/L (5%) and 4.43 mg/L (11-12%). Single cases of diaphragmatic hernia or missing ribs were observed at 1.47, 2.95, and 4.43 mg/L. External variations, limited to club foot, were only observed in the control group. No treatment-related effects were observed on the incidence of skeletal or visceral variations. The NOAEC for

maternal and developmental toxicity was identified as 1.47 mg/L by the study authors based on decreases to maternal body weight and fetal body weight in the two highest dose groups. The teratogenicity NOAEC was identified as 4.43 mg/L by the study authors based on the lack of teratogenic effects observed with treatment. Based on the correlation between the decreased maternal body weight and fetal body weight, ToxServices concluded that the decreased fetal weight is likely a result of the decreased maternal body weight and food consumption and not a direct effect of the treatment. Therefore, ToxServices assigned a developmental toxicity NOAEC of 4.43 mg/L.

- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014b
    - A prenatal developmental toxicity study conducted according to OECD 414 was performed with pregnant female Sprague-Dawley rats (17-24/dose group) administered whole body inhalation exposures to 1,3,5-trimethylbenzene (99% purity) vapor at 0, 492, 1,470, 2,950, or 5,900 mg/m^3 (equivalent to 0, 0.492, 1.47, 2.95, and 5.90 mg/L, respectively) for 6 hours/day on GD 6-20. The animals were sacrificed on GD 21. The maternal observations included clinical signs of toxicity, food consumption, and ovarian and uterine content. Fetal examinations consisted of evaluating the incidences of external, visceral, and skeletal malformations. No maternal deaths or clinical signs of toxicity were observed with treatment. Maternal body weight decreased significantly during the second half of the exposure period at 1.47 mg/L and throughout the entire exposure period for 2.95 and 5.90 mg/L. Significant decreases in food consumption were observed at concentrations of 1.47 mg/L and greater. No treatment-related effects were observed on the number of implantation sites or live fetuses, or on the incidences of post-implantation loss and resorption. A concentration-dependent decrease in fetal body weight was observed in males at 2.95 mg/L and in males and females at 5.9 mg/L. Diaphragmatic hernia was observed in one fetus at 0.492 mg/L and in one fetus at 2.95 mg/L. The incidence of fetuses with incomplete sternbral ossification was slightly but not statistically significantly increased in the high concentration group. The NOAEC for maternal toxicity was identified as 0.492 mg/L by the study authors based on decreased body weights and food consumption at 1,470 mg/L and higher. The developmental toxicity NOAEC was identified as 1.47 mg/L by the study authors based on decreases to fetal body weight in the two highest dose groups. The teratogenicity NOAEC was identified as 5.9 mg/L by the study authors based on the lack of teratogenic effects observed with treatment. Based on the correlation between the decreased maternal body weight and fetal body weight, ToxServices concluded that the decreased fetal weight is likely a result of the decreased maternal body weight and food consumption, and not a direct effect of the treatment. Therefore, ToxServices assigned a developmental toxicity NOAEC of 5.9 mg/L.

Endocrine Activity (E) Score (H, M, or L): DG
Trimethylbenzenes were assigned a score of Data Gap for endocrine disruption based on the lack of data identified for this endpoint.

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

        - Not listed on any screening lists for this endpoint.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- 1,2,4-Trimethylbenzene, CAS #95-63-6 –
    - High Throughput Screening (HTS) Data –
        - HTS data were identified for 1,2,4-trimethylbenzene using PubChem (http://pubchem.ncbi.nlm.nih.gov/).
        - The data included the following results:
            - 1,2,4-Trimethylbenzene was active in 0/6 androgen receptor agonist assays and 0/12 androgen receptor antagonist assays.
            - 1,2,4-Trimethylbenzene was active in 0/6 estrogen receptor-alpha agonist assays and 0/12 estrogen receptor-alpha antagonist assays.
            - 1,2,4-Trimethylbenzene was active in 0/2 thyroid receptor agonist assays and 0/6 thyroid receptor antagonist assays.
            - The activity of 1,2,4-trimethylbenzene towards the thyroid stimulating hormone receptor was not evaluated.
- 1,3,5-Trimethylbenzene, CAS #108-67-8 –
    - High Throughput Screening (HTS) Data –
        - HTS data were identified for 1,3,5-trimethylbenzene using PubChem (http://pubchem.ncbi.nlm.nih.gov/).
        - The data included the following results:
            - 1,3,5-Trimethylbenzene was active in 1/6 androgen receptor agonist assays and 0/12 androgen receptor antagonist assays.
            - 1,3,5-Trimethylbenzene was active in 0/6 estrogen receptor-alpha agonist assays and 0/12 estrogen receptor-alpha antagonist assays.
            - 1,3,5-Trimethylbenzene was active in 0/2 thyroid receptor agonist assays and 0/6 thyroid receptor antagonist assays.
            - The activity of 1,3,5-trimethylbenzene towards the thyroid stimulating hormone receptor was not evaluated.
- These data are insufficient to assign a score for endocrine activity.

Group II and II* Human Health Effects (Group II and II* Human)

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

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): M

Trimethylbenzenes were assigned a score of Moderate for acute toxicity based on a 4-hour vapor inhalation LC_{50} value of 18 mg/L. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when 4-hour inhalation LC_{50} values are greater than 10 to 20 mg/L for vapor (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:*
        - GHS Hazard Statement H332 – harmful if inhaled
        - EU Risk Phrase R20 – harmful by inhalation

    - *Screening:*
        - GHS New Zealand Category 6.1D (inhalation) (equivalent to GHS Category 4 inhalation toxicant) – acutely toxic
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - ChemIDplus 2014
        - *Oral*: LD_{50} (rat) = 5,000 mg/kg
        - *Inhalation*: LC_{50} (rat) = 18,000 mg/m^3 = 18 mg/L
    - ECHA 2014a
        - *Oral*: LD_{50} (male rat) = 6,000 mg/kg (GLP-compliant, EU Method B.1)
        - *Oral*: LD_{50} (Charles River CD (CRL:COBS CD (SD) BR) rats) = 3,550 mg/kg for males and 3,280 mg/kg for females (EU Method B.1)
        - *Oral*: LD_{50} (rat) = 5,000 mg/kg
        - *Inhalation*: 12-hour whole body vapor LC_{50} (Wistar rat) = 9,833 mg/m^3 (equivalent to 9.833 mg/L)
        - *Inhalation*: 4-hour vapor LC_{50} (rat) = 18,000 mg/m^3 (equivalent to 18 mg/L)
- 1,3,5-Trimethylbenzene, CAS #108-67-8
    - ECHA 2014b
        - *Inhalation*: 4-hour vapor LC_{50} (rat) = 24,000 mg/m^3 (equivalent to 24 mg/L)
- Trimethylbenzenes, CAS #25551-13-7
    - ECHA 2014a
        - *Oral*: LD_{50} (rat) = 8,970 mg/kg

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)* (vH, H, M, or L): M**
Trimethylbenzenes were assigned a score of Moderate for systemic toxicity (single dose) based on authoritative lists. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are associated with GHS Hazard Statement H335 or EU Risk Phrase R37 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:*
        - GHS Hazard Statement H335 – may cause respiratory irritation (CAS #95-63-6, 108-67-8)
        - EU Risk Phrase R37 – irritating to respiratory system (CAS #95-63-6, 108-67-8)
    - *Screening:*
        - GHS Japan Category 3 specific target organs/systemic toxicity following single exposure (CAS #95-63-6, 108-67-8)
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - ECHA 2014a
        - *Oral*: In the acute oral toxicity study that identified an oral LD_{50} value of 6,000 mg/kg, clinical signs of toxicity observed at all dose levels (3,510-10,140 mg/kg) included lethargy and ptosis. Ataxia and piloerection were observed at 5,000 mg/kg and greater. Prostration, emaciation, flaccid muscle tone, tachypnea, chromorhinorrhea (discharge of pigmented secretion from the nose), and chromodacryorrhea (colored tears) were observed in the two highest dose levels.
        - *Oral*: In the acute oral toxicity study that identified oral LD_{50} values of 3,550 mg/kg for males and 3,280 mg/kg for females, slight inactivity was noted at 1,470 mg/kg. With increasing dose, the animals exhibited salivation, inactivity, incoordination, rough coat and/or piloerection, arched back, prostration, and Straub tail (only in

higher dose levels). Some animals also exhibited nasal discharge and tremors. The animals that survived to the scheduled sacrificed gained body weight through the observation period. At necropsy, animals that survived to the scheduled sacrifice exhibited dark lungs, dilated renal pelvis, white solid material in the bladder, and discolored and friable livers. Animals that died after dosing exhibited bright red, dark, mottled lungs, greatly distended urinary bladders, urine with slight yellow fluorescence, yellow gastrointestinal tract with mucous-like consistency, prominent and engorged mesenteric vessels, stomachs were distended with food, pale, mottled, dark, nutmeg livers, thymus with dark spots, fat stained yellow, and evidence of hemorrhagic vessels in the bladder wall. The doses at which these effects were observed were not specified.

- *Inhalation:* In the acute inhalation toxicity study that identified an LC_{50} of 9.833 mg/m^3, no adverse clinical signs of toxicity were observed and no treatment-related histopathological effects were noted on the lungs, liver, kidneys, spleen, or adrenal glands.

- In summary, the oral and dermal studies did not identify significant systemic toxicity effects or the effects were observed at doses greater than 2,000 mg/kg. Therefore, ToxServices could not assign a GHS classification for systemic toxicity (single dose) (UN 2013). Therefore, ToxServices relied on the EU H335 and R37 to assign the score for this endpoint.

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

Trimethylbenzenes were assigned a score of Low for systemic toxicity (repeated dose) based on an oral NOAEL of 600 mg/kg/day in a 90-day study performed with 1,3,5-trimethylbenzene and no systemic toxicity observed at the highest inhalation concentrations in studies performed with 1,2,4-trimethylbenene and 1,2,3-trimethylbenzene. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when oral NOAELs are greater than 100 mg/kg/day (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - GHS Japan Category 2 specific target organs/systemic toxicity following repeated exposure
    - GHS New Zealand Category 6.9B (inhalation) (equivalent to GHS Category 2 specific target organ systemic toxicant) – harmful to human target organs or systems
- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014a
    - *Oral*: Sprague-Dawley CD rats (10/sex/dose group, an additional 10 animals in the high dose for recovery satellite group) for controls, low, and mid groups. Twenty/sex for high dose groups were administered oral doses of 1,3,5-trimethylbenzene (99.2% purity) in corn oil at 0, 50, 200, or 600 mg/kg/day via gavage 5 days/week for 90-91 days. The equivalent doses for a 7-day/week exposure frequency were 0, 35.7, 143, and 429 mg/kg/day. A satellite group of 10 animals/sex was administered the high dose for the same amount of time and then maintained for an additional 28 exposure-free days. Animals were evaluated for clinical signs of toxicity, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. High dose animals exhibited discolored inguinal fur, wet inguinal fur, and salivation. These effects were not observed in the recovery animals at the end of the treatment-free period. Cumulative body weight gain was decreased by approximately 11% in high

dose males. This effect was considered to be reversible since it was not observed at the end of the recovery period in the satellite group. No treatment-related effects were observed on food consumption or hematology parameters. Serum phosphorus levels increased in high dose males and females, but the increase was not evident at the end of the recovery period. Absolute liver weight in high dose females and relative liver weights in high dose males and females were increased over control values. Relative kidney weight also increased in high dose males. No treatment-related effects were noted on gross pathological and histopathological observations. The study authors identified a NOAEL of 600 mg/kg/day (equivalent to 429 mg/kg/day for a 7-day/week exposure period) based on the lack of treatment-related effects on histopathology.

- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a
    - *Inhalation*: Outbred Imp.WIST rats (10/sex/concentration group, additional 10/sex in the high concentration group were maintained for an additional 2 week treatment-free recovery period) were administered whole body inhalation exposures to 1,2,4-trimethylbenzene (greater than 97% purity) vapor at 0, 123, 492, or 1,230 mg/m^3 (equivalent to 0, 0.123, 0.492, and 1.23 mg/L, respectively) for 6 hours/day, 5 days/week for 3 months. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.88 mg/L, respectively. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. No treatment-related effects on clinical signs of toxicity, body weight, food consumption, organ weights, or gross pathology were observed. Hematological effects included decreased red blood cells and increased white blood cells in high concentration males, decreased reticulocyte counts in high concentration females, decreased clotting time in mid and high concentration females. At the end of the exposure period, only red blood cell counts remained different from controls. Increased sorbitol dehydrogenase activity was observed in all treated males. This effect was considered to be related to respiratory irritation. No significant histopathological changes were observed in the upper respiratory tract with treatment. In the mid and high dose groups there was an increased incidence of peribronchial, lung parenchymal, and perivascular lymphocytic infiltrations. The systemic toxicity NOAEC was identified as 1,230 mg/m^3 (equivalent to 0.88 mg/L for a 7-day/week exposure frequency) based on the lack of systemic toxicity at the highest concentration tested.
    - *Inhalation:* Male Wistar IMP:DAK outbred rats (10/dose group) were administered whole body inhalation exposures of 1,2,4-trimethylbenzene (greater than 97% purity) vapor at 0, 123, 492, and 1,230 mg/m^3 (equivalent to 0, 0.123, 0.492, and 1.23 mg/L) for 6 hours/day, 5 days/week for 90 days. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.88 mg/L, respectively. The animals were evaluated for clinical signs of toxicity, body weights, and bronchiolar lavage (BAL). No treatment-related effects were observed on clinical signs of toxicity or body weight. The BAL revealed an increase in the total number of macrophages, polymophonuclear leucocytes, and lymphocytes at all 3 concentrations relative to controls, indicative of mild respiratory irritation. Total protein, acid phosphatase activity, and lactate dehydrogenase activity also increased in the BAL of exposed groups. The study authors identified a systemic toxicity

NOAEC of 1.23 mg/L (equivalent to 0.88 mg/L for a 7-day/week exposure frequency) based on the lack of systemic toxicity at the highest concentration tested.

- 1,2,3-Trimethylbenzene, CAS #526-73-6
  - ECHA 2014a
    - *Inhalation*: A repeated dose inhalation exposure study conducted according to OECD 413 was performed with outbred Imp:WISTAR rats (10/sex/dose group, additional 10/sex in high concentration group for 1 month long treatment-free recovery period) administered whole body exposures to 1,2,3-trimethylbenzene (greater than 97% purity) vapor at 0, 123, 492, or 1,230 mg/m^3 (equivalent to 0, 0,123, 0.492, and 1.23 mg/L, respectively) for 6 hours/day, 5 days/week for 3 months. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.88 mg/L, respectively. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. No treatment-related effects were observed on clinical signs of toxicity, body weight, food consumption, or gross pathology. In the high concentration group, a decrease in red blood cell counts and increase in reticulocyte counts were observed in males, and decreases in segmented neutrophil counts and increases in lymphocyte counts were observed in both sexes. Increases in reticulocyte counts were observed in females of all treatment groups. After the recovery period, the hematology parameters returned to control values. Increases in sorbitol dehydrogenase activity were observed in high concentration males and increases in alkaline phosphatase activity were observed in mid and high concentration females. A significant increase in the relative liver weight was observed in high concentration males. No histopathological changes in the upper respiratory tract, urinary tract, spleen, digestive system, endocrine glands, or gonads were observed with treatment. An increased number of goblet cells in the bronchi of mid and high concentration females and an increase in the intensity of lung perivascular and interstitial infiltration of high concentration males were observed. These effects were considered to represent an inflammatory response as a result of respiratory irritation. The study authors identified a systemic toxicity NOAEC of 1.23 mg/L (equivalent to 0.88 mg/L for a 7-day/week exposure frequency) based on the lack of systemic toxicity at the highest concentration tested.

Neurotoxicity (N)

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

Trimethylbenzenes were assigned a score of Very High for neurotoxicity (single dose) based on EC_{50} values of 4.69 mg/L and 5.678 mg/L for rotarod performance and pain sensitivity, respectively, in rats administered single exposures to 1,2,4-trimethylbenzene vapor. GreenScreen® criteria classify chemicals as a Very High hazard for neurotoxicity (single dose) when neurotoxic effects are observed at vapor concentrations up to 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a

- In an acute neurotoxicity assessment, male Wistar rats (10/dose group) were administered single exposures to 1,2,4-trimethylbenzene (greater than 97% purity) vapor at 250 to 2,000 ppm (equivalent to 1.229 to 9.832 mg/L[6]) for 4 hours. The animals were evaluated for rotarod performance and hot plate (pain) behavior. The EC_{50} for rotarod performance was 954 ppm (equivalent to 4.69 mg/L) and the EC_{50} for pain sensitivity was 1,155 ppm (equivalent to 5.678 mg/L).

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

Trimethylbenzenes were assigned a score of High for neurotoxicity (repeated dose) based on a LOAEC of 0.088 mg/L in a 3-month study of male Wistar rats exposed to 1,2,4-trimethylbenzene vapor. GreenScreen® criteria classify chemicals as a High hazard for neurotoxicity (repeated dose) when the neurotoxicity LOAEC is up to vapor concentrations of 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a
    - A neurobehavioral study was performed with male Wistar rats (8/dose group) exposed to 1,2,4-trimethylbenzene (greater than 98% purity) vapor at 125, 1,250, or 5,000 mg/m^3 (equivalent to 0.125, 1.25, or 5.0 mg/L, respectively) for 8 hours/day for 1-3 days. The rats were evaluated in a functional observation battery (FOB) and assessments of motor activity and visual discrimination performance were performed. No treatment-related effects were observed in the FOB. Decreased motor activity was observed after the third 8-hour exposure, but this effect was not considered to be treatment-related as a similar decrease was not observed after the first 8-hour exposure. An increased frequency of long latencies to response was observed in the visual discrimination performance evaluation at 5.0 mg/L. The effect was greater after the first 8-hour exposure than after the third 8-hour exposure, correlating with the pharmacokinetic results that indicated that the brain concentrations of 1,2,4-trimethylbenzene were greater after the first 8-hour exposure than after the third 8-hour exposure.
    - Male Wistar rats (11 in treatment group, 10 in control) were exposed to 1,2,4-trimethylbenzene (purity not specified) vapor at 100 ppm (equivalent to 0.492 mg/L[7]) for 6 hours/day, 5 days/week for 4 weeks. The equivalent concentration for a 7-day/week exposure frequency was 0.351 mg/L. Beginning 14 days into the exposure period, the rats were evaluated in a radial arm maze (short-term spatial memory), an open field test (spontaneous activity), conditioned passive and active avoidance tests (long-term memory and learning ability), and a hot plate test (responsiveness to thermal stimulus). No treatment-related effects were observed on the radial maze performance. Increased locomotor activity in the open field test, increased latency of the paw-lick response in the hot plate test, and impaired acquisition of passive

[6] The equivalent concentration in mg/L was determined using the formula (mg/L) = [(ppm) x (molecular weight)]/ 24,450. The molecular weight of 1,2,4-trimethylbenzene is 120.194 g/mol.
[7] The equivalent concentration in mg/L was determined using the formula (mg/L) = [(ppm) x (molecular weight)]/ 24,450. The molecular weight of 1,2,4-trimethylbenzene is 120.194 g/mol.

avoidance response were observed. A deficit in learning but not in retention of the active avoidance response was observed. The study authors concluded that the treatment did not produce cognitive impairment but rather a decreased ability to inhibit locomotor response.

- Male Wistar rats (9-10/dose group) were exposed to 1,2,4-trimethylbenzene (purity not specified) vapor at 0, 123, 491, or 1,227 mg/m^3 (equivalent to 0, 0.123, 0.491, and 1.227 mg/L, respectively) for 6 hours/day, 5 days/week for 4 weeks. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.876 mg/L, respectively. The animals were evaluated for body weight and underwent electroencephalography (EEG) analysis. No treatment-related effects were observed on body weight or on spontaneous cortical spike-wave discharges (swd) during EEG analysis. A NOAEC of 1.227 mg/L (equivalent to 0.876 mg/L for a 7-day/week exposure frequency was identified by ToxServices.
- Male Wistar rats (10/dose group) were exposed to 1,2,4-trimethylbenzene (greater than 97% purity) vapor at 0, 25, 100, or 250 ppm (equivalent to 0, 0.123, 0.492, and 1.229 mg/L, respectively[8]) for 6 hours/day, 5 days/week for 3 months. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.878 mg/L, respectively. The animals were evaluated for rotarod performance and hot plate (pain) behavior. A concentration-dependent disturbance in the rotarod performance and a decrease in pain sensitivity were observed with treatment. After two exposure-free weeks, the rotarod performance behavior was not fully recovered. The LOAEC was identified as 25 ppm (0.088 mg/L for a 7-day/week exposure frequency) by the study authors.

- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014b
    - Male Wistar rats (11 in treatment group, 10 in control) were administered inhalation exposures to 1,3,5-trimethylbenzene (purity not specified) vapor at 100 ppm (equivalent to 0.492 mg/L[9]) for 6 hours/day, 5 days/week for 4 weeks. The equivalent concentration for a 7-day/week exposure frequency was 0.351 mg/L. Beginning 14 days into the exposure period, the rats were evaluated in a radial arm maze (short-term spatial memory), an open field test (spontaneous activity), conditioned passive and active avoidance tests (long-term memory and learning ability), and a hot plate test (responsiveness to thermal stimulus). No treatment-related effects were observed on body weight or on the radial maze performance. Increased locomotor activity in the open field test, increased latency of the paw-lick response to heat in the hot plate test, and impaired acquisition of the passive avoidance response were observed with treatment. These effects were indicative of a decreased ability to inhibit locomotor response and not of cognitive impairments.
    - Male LOD:WIST outbred rats (12/dose group) were administered inhalation exposures to 1,3,5-trimethylbenzene (FLUKA grade) vapor at 0, 25, 100, or 250 ppm (equivalent to 0, 0.125, 0.500, and 1.25 mg/L, respectively) for 6 hours/day, 5 days/week for 1 month. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.089, 0.357, and 0.893 mg/L, respectively. The animals were evaluated in the radial maze, open field, step-down passive avoidance, hot plate, and

[8] The equivalent concentrations in mg/L were determined using the formula (mg/L) = [(ppm) x (molecular weight)]/ 24,450. The molecular weight of 1,2,4-trimethylbenzene is 120.194 g/mol.
[9] The equivalent concentration in mg/L was determined using the formula (mg/L) = [(ppm) x (molecular weight)]/ 24,450. The molecular weight of 1,3,5-trimethylbenzene is 120.194 g/mol.

conditioned active avoidance reaction tests. No treatment-related effects were observed on body weight, radial maze performance, or open field behavior. The persistence of the passive avoidance reaction was shorter in all treatment groups, with additional trials required to produce the active avoidance reaction observed in the controls. The mid concentration group appeared to be more fearful of testing on the hot plate during the second day of testing. No evidence of a concentration-response relationship was observed for these effects. Based on the lack of a concentration-response relationship, the study authors identified a NOAEC of 1.25 mg/L (0.893 mg/L for a 7-day/week exposure frequency).

- 1,2,3-Trimethylbenzene, CAS #526-73-8
  - HSDB 2008c
    - Rats (strain, sex, and number not specified) were administered inhalation exposures of 1,2,3-trimethylbenzene (purity not specified) at 0, 25, 100, or 250 ppm (equivalent to 0, 0.123, 0.492, and 1.229 mg/L, respectively[10]) for 6 hours/day, 5 days/week for 4 weeks. The equivalent concentrations for a 7-day/week exposure frequency were 0, 0.088, 0.351, and 0.878 mg/L, respectively. The animals were evaluated on their radial maze performance, open field activity, passive and active avoidance learning, and on the paw-lick response to heat in the hot plate test. No treatment-related effects were observed in the open field or radial maze assessments. Rats exposed to the low or mid concentrations, but not the high concentration, exhibited impaired learning of the passive avoidance. In the mid concentration group, acquisition of the two-way active avoidance in the shuttle box was slower and an increased latency in the paw-lick response to heat lasted for a longer period of time compared to control animals. No further details were provided. Based on the lack of a concentration-response, ToxServices identified a NOAEC of 1.229 mg/L (0.878 mg/L for a 7-day/week exposure frequency).
- The most conservative result from repeated dose neurotoxicity tests was the LOAEC of 25 ppm (0.088 mg/L for a 7-day/week exposure frequency) obtained in the 3-month study of male Wistar rats were exposed to 1,2,4-trimethylbenzene vapor. This value was used to assign the score for this endpoint.

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

Trimethylbenzenes were assigned a score of Low for skin sensitization based on the lack of positive reactions observed in a guinea pig maximization test performed with the surrogate aromatic naphtha, type I. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- No data for trimethylbenzenes were identified for this endpoint.
- Surrogate: Aromatic Naphtha, Type I (CAS #64742-95-6).
  - ECHA 2014a
    - A non-GLP-compliant guinea pig maximization test conducted according to OECD 406 was performed with 'P' strain guinea pigs (10/sex for treatment, 5/sex for

[10] The equivalent concentrations in mg/L were determined using the formula (mg/L) = [(ppm) x (molecular weight)]/ 24,450. The molecular weight of 1,2,3-trimethylbenzene is 120.194 g/mol.

controls) administered dermal applications of aromatic naphtha, type I (identified as essentially C9 isomers, particularly trimethylbenzenes). An intradermal injection of 0.1% w/v in corn oil was administered followed by a topical application of a 50% w/v solution in corn oil. The animals were then challenged with a topical application of a 25% w/v solution in corn oil. No details on temporal spacing of doses were provided. The reactions were scored 24 and 48 hours after the challenge application. No positive reactions were observed following the challenge dose. The study authors concluded that aromatic naphtha, type I was not dermally sensitizing.

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

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

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): H
1,2,4-Trimethylbenzene was assigned a score of High for skin irritation/corrosivity based on ToxServices classifying 1,3,5-trimethylbenzene as a GHS Category 2 skin irritant. GreenScreen® criteria classify chemicals as a High hazard for skin irritation/corrosivity when a GHS Category 2 skin irritant classification is assigned (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - GHS Hazard Statement H315 – causes skin irritation (CAS #95-63-6)
    - EU Risk Phrase R36/37/38 – irritating to eyes, respiratory system and skin (CAS #95-63-6)
  - *Screening:*
    - GHS New Zealand Category 6.3B (equivalent to GHS Category 3 skin irritant) – mildly irritating to the skin (CAS #95-63-6, 108-67-8)
    - GHS Japan Category 2B – skin irritant (CAS #108-67-8)
- 1,3,5-trimethylbenzene, CAS #108-67-8
  - ECHA 2014a
    - A dermal irritation test conducted according to EU Method B.4 was performed with New Zealand White rabbits (5-6 total, sex not specified) administered topical applications of 0.5 mL undiluted 1,3,5-trimethylbenzene (purity not specified) to shaved skin under occlusive dressing for 4 hours. The skin reactions were scored at 1, 24, 48, and 72 hours after removal of the dressing. The mean erythema score was 2.33. The authors concluded that 1,3,5-trimethylbenzene was irritating to skin.
      - Based on this result, ToxServices classified 1,3,5-trimethylbenzene as a GHS Category 2 skin irritant. GHS Category 2 skin irritants include those that produce mean scores of ≥ 2.3 and ≤ 4.0 for erythema or edema in at least 2 of 3 tested animals from gradings at 24, 48, and 72 hours after dressing/patch removal (UN 2013).
    - A dermal irritation test conducted according to EU Method B.4 was performed with New Zealand White rabbits (5-6 total, sex not specified) administered topical

applications of 0.5 mL 1,3,5-trimethylbenzene (purity not specified) in sweet almond oil at 5%, 10%, 25%, 50%, or 100% to shaved skin under occlusive dressing for 4 hours. The skin reactions were scored at 1, 24, 48, and 72 hours after removal of the patch. Concentrations greater than 25% were found to be irritating to rabbit skin in this study.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): H
Trimethylbenzenes were assigned a score of High for eye irritation/corrosivity based on authoritative lists. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are associated with GHS Hazard Statement H319 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - GHS Hazard Statement H319 – causes serious eye irritation (CAS #95-63-6)
    - EU Risk Phrase R36/37/38 – irritating to eyes, respiratory system and skin (CAS #95-63-6)
  - *Screening:*
    - GHS New Zealand Category 6.4A (equivalent to GHS Category 2 eye irritant) – irritating to the eye (CAS #95-63-6, 108-67-8)
    - GHS Japan Category 2B – serious eye damage/eye irritation (CAS #108-67-8)
- No data for trimethylbenzenes were identified for this endpoint.
- Surrogate: Aromatic Naphtha, Type I (CAS #64742-95-6).
  - ECHA 2014a
    - A non-GLP-compliant ocular irritation test conducted according to OECD 405 was performed with New Zealand White rabbits (2/sex) administered ocular instillations of 0.2 mL undiluted aromatic naphtha, type I (described as essentially C9 isomers, especially trimethylbenzenes). The animals were observed for 7 days following the instillation. After 30 minutes, slight to moderate conjunctival redness was observed in all 4 animals and slight to moderate chemosis was observed in 3/4 rabbits. Conjunctival discharge was evident in one rabbit at 30 minutes and at 24 hours but did not persist beyond that time point. Conjunctival effects did not persist and no chemosis was observed after 24 hours. Very slight redness was observed in 2 rabbits at 24 hours but all redness resolved by 48 hours. No effects to the cornea or iris were observed. The study authors concluded that aromatic naphtha, type I was not irritating to eyes.

<u>Ecotoxicity (Ecotox)</u>

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): H
Trimethylbenzenes were assigned a score of High for acute aquatic toxicity based on acute aquatic toxicity values as low as 3.6 mg/L for 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene and association with R51/53. GreenScreen® criteria classify chemicals as a High hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 1 to 10 mg/L and/or they are associated with R51/53 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:*
    - EU Risk Phrase R51/53 – toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (CAS #95-63-6, 108-67-8)
  - *Screening:*

        - GHS Japan Category 2 – hazardous to the aquatic environment (CAS #95-63-6, 108-67-8)
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - ECHA 2014a
        - 96-hour LC_{50} (*Pimephales promelas*, fathead minnow) = 7.72 mg/L
        - 96-hour LC_{50} (*Oryzias latipes*, Japanese rice fish) = 7.72 mg/L
        - 48-hour LC_{50} (*Daphnia magna*) = 3.6 mg/L (similar to OECD 202)
        - 24-hour LC_{50} (*Artemia* species, brine shrimp) = 12 mg/L
- 1,3,5-Trimethylbenzene, CAS #108-67-8
    - ECHA 2014b
        - 96-hour LC_{50} (*Carassius auratus*, goldfish) = 12.52 mg/L
        - 48-hour LC_{50} (*Oryzias latipes*, Japanese rice fish) = 8.6 mg/L
        - 48-hour LC_{50} (Daphnia magna) = 6 mg/L (similar to OECD 202)
        - 48-hour biomass EC_{50} (*Desmodesmus subspicatus*, green algae) = 25 mg/L (DIN 38 412, part 9)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): H
Trimethylbenzenes were assigned a score of High for chronic aquatic toxicity based on a 21-day reproduction NOEC of 0.4 mg/L in daphnia exposed to 1,3,5-trimethylbenzene. GreenScreen® criteria classify chemicals as a High hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 0.1 to 1.0 mg/L (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:*
        - GHS Hazard Phrase H411 – toxic to aquatic life with long-lasting effects (CAS #95-63-6, 108-67-8)
    - *Screening:*
        - GHS Japan Category 2 – hazardous to the aquatic environment (CAS #95-63-6, 108-67-8)
        - GHS New Zealand Category 9.1B (fish, crustacean) (equivalent to GHS Category 2 chronic aquatic toxicant) – very ecotoxic in the aquatic environment (CAS #95-63-6, 108-67-8)
        - GHS New Zealand Category 9.1C (fish, algae) (equivalent to GHS Category 3 chronic aquatic toxicant) – harmful in the aquatic environment (CAS #108-67-8)
- 1,3,5-Trimethylbenzene, CAS #108-67-8
    - ECHA 2014b
        - 21-day reproduction NOEC (*Daphnia magna*) = 0.4 mg/L
        - 48-hour biomass EC_{10} (*Desmodesmus subspicatus*, green algae) = 8.1 mg/L (DIN 38 412, part 9)

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *H*
Trimethylbenzenes were assigned a score of High for persistence based on predicted half-lives of 75 days for trimethylbenzenes in soil, their primary environmental compartment. GreenScreen® criteria classify chemicals as a High hazard for persistence when chemicals have a half-life of greater than 60 to 180 days in soil when soil is their primary environmental compartment (CPA 2012a). The confidence in this score is adjusted as it is based on modeling.

- Authoritative and Screening Lists
  - *Authoritative:*
    - Not listed on any authoritative lists for this endpoint.
  - *Screening:*
    - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
  - ECHA 2014a
    - A biodegradation test was performed with non-adapted, activated domestic sludge from three sources exposed to 1,2,4-trimethylbenzene (purity not specified) at 500 mg/L for 120 hours. The level of degradation was 12.5-75% depending on the source of the sludge.
    - A biodegradation test was performed with pooled bacteria cultures, including one cultured specifically to digest 1,2,4-trimethylbenzene, exposed to greater than 0.02 to 0.2 mg/L for up to 4 days. The level of degradation was 100% after 1 day.
    - A ready biodegradability test conducted according to OECD 301 C (Modified MITI test) was performed with activated sludge (adaptation not specified) exposed to 1,2,4-trimethylbenzene (purity not specified) at 100 mg/L for 28 days. At the end of the exposure period, the level of degradation was at least 4% to 18% based on BOD. 1,2,4-trimethylbenzene was not readily biodegradable in this test.
    - A biodegradation test was performed with natural sediment and water exposed to 1,2,4-trimethylbenzene (purity not specified) at 1-4 mg/L for 13 days under anaerobic conditions. At the end of the exposure period, the level of degradation was 96%.
- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014b
    - A non-GLP-compliant biodegradation test was performed with activated sludge acclimatized to benzene exposed to 1,3,5-trimethylbenzene (analytical grade) at 500 mg/L for 192 hours. At the end of the exposure period, the level of degradation was 0%.
    - A ready biodegradability test conducted according to OECD 301 C was performed with activated sludge exposed to 1,3,5-trimethylbenzene (purity not specified) at 100 mg/L for 2 weeks. At the end of the exposure period, the level of degradation was 0%.
    - A biodegradability test was performed with activated domestic sludge (adaptation not specified) exposed to 1,3,5-trimethylbenzene (purity not specified) at 500 mg/L for 180 hours. At the end of the exposure period the level of degradation was 0%.
- Based on the lack of sufficient data to classify trimethylbenzenes for persistence, ToxServices performed modeling with EPI Suite to estimate the persistence of trimethylbenzenes (see Appendix H).
  - U.S. EPA 2012
    - 1,2,4-Trimethylbenzene, CAS #95-63-6
      - The BIOWIN modeling Ready Biodegradable Predictor indicates that 1,2,4-trimethylbenzene is not expected to be readily biodegradable. Fugacity modeling predicts 63.8% will partition to soil with a half-life of 75 days, 31.9% will partition to water with a half-life of 37.5 days, and 3.22% will partition to air with a half-life of 7.9 hours.
    - 1,3,5-Trimethylbenzene, CAS #108-67-8

        - The BIOWIN modeling Ready Biodegradable Predictor indicates that 1,3,5-trimethylbenzene is not expected to be readily biodegradable. Fugacity modeling predicts 57.5% will partition to soil with a half-life of 75 days, 38.8% will partition to water with a half-life of 37.5 days, and 2.39% will partition to air with a half-life of 4.46 hours.
    - 1,2,3-Trimethylbenzene, CAS #526-73-8
        - The BIOWIN modeling Ready Biodegradable Predictor indicates that 1,2,3-trimethylbenzene is not expected to be readily biodegradable. Fugacity modeling predicts 69.9% will partition to soil with a half-life of 75 days, 26.6% will partition to water with a half-life of 37.5 days, and 2.57% will partition to air with a half-life of 7.85 hours.
- As all three trimethylbenzene isomers are expected to have soil as their primary environmental compartment with a half-life of 75 days, ToxServices used this information to assign a score of High for persistence.

Bioaccumulation (B) Score (vH, H, M, L, or vL): L
Trimethylbenzenes were assigned a score of Low for bioaccumulation based on BCF values of up to 275 for 1,2,4-trimethylbenzene and up to 342 for 1,3,5-trimethylbenzene. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when BCF values are greater than 100 to 500 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:*
        - Not listed on any authoritative lists for this endpoint.
    - *Screening:*
        - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - ECHA 2014a
        - A bioaccumulation test was performed with *Cyprinus carpio* (carp) exposed to 1,2,4-trimethylbenzene (purity not specified) at 0.02 or 0.2 mg/L for 8 weeks. The BCF values for the 0.02 mg/L treatment were 31 to 207 and the BCF values for the 0.2 mg/L treatment were 33 to 275.
- 1,3,5-Trimethylbenzene, CAS #108-67-8
    - ECHA 2014b
        - A bioaccumulation test was performed with *Cyprinus carpio* (carp) exposed to 1,2,4-trimethylbenzene (purity not specified) at 15 ppb or 150 ppb for 10 weeks. The BCF values for the 15 ppb treatment were 42 to 328 and the BCF values for the 150 ppb treatment were 20 to 342.

<u>Physical Hazards (Physical)</u>

Reactivity (Rx) Score (vH, H, M, or L): *L*
Trimethylbenzenes were assigned a score of Low for reactivity based on the surrogate triethylene glycol not being classified as reactive under GHS criteria (2013). GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classification can be assigned (CPA 2012a). The confidence in the classification is adjusted as it is not based on data or an authoritative list.

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

    - *Screening:*
        - Not listed on any screening lists for this endpoint.
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - Sigma-Aldrich 2014a
        - A material safety data sheet for 1,2,4-trimethylbenzene states that it has a reactivity rating of 0 from the NFPA ("Normally stable, even under fire exposure conditions, and is not reactive with water") and HMIS ("Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives").
- 1,3,5-Trimethylbenzene, CAS #108-67-8
    - Sigma-Aldrich 2014b
        - A material safety data sheet for 1,3,5-trimethylbenzene states that it has a reactivity rating of 0 from the NFPA ("Normally stable, even under fire exposure conditions, and is not reactive with water") and HMIS ("Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives").
- 1,2,3-Trimethylbenzene, CAS #526-73-8
    - Sigma-Aldrich 2014c
        - A material safety data sheet for 1,2,3-trimethylbenzene states that it has a reactivity rating of 0 from the NFPA ("Normally stable, even under fire exposure conditions, and is not reactive with water") and HMIS ("Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives").
    - Based on the MSDSs identified above stating that that the trimethylbenzene isomers are nonreactive, ToxServices did not classify trimethylbenzenes as reactive chemicals based on GHS criteria (UN 2013).

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

Trimethylbenzenes were assigned a score of Moderate for flammability based on ToxServices classifying 1,2,4-trimethylbenzene and 1,3,5-trimethylbenzene as GHS Category 3 flammable liquids. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when a classification of GHS Category 3 flammable liquid is assigned (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:*
        - GHS Hazard Statement H226 – flammable liquid and vapor (CAS #95-63-6, 108-67-8)
        - EU Risk Phrase R10 – flammable liquid (CAS #95-63-6, 108-67-8)
    - *Screening:*
        - Quebec CSST WHMIS classifications Class B3 – combustible liquids (CAS #95-63-6, 108-67-8, 526-73-8)
    - *Other*:
        - GHS New Zealand Category 3.1C (equivalent to GHS Category 3) – flammable liquids: medium hazard (CAS #95-63-6, 108-67-8, 526-73-8)
        - GHS Japan Category 3 flammable liquid (CAS #95-63-6, 108-67-8)
- 1,2,4-Trimethylbenzene, CAS #95-63-6
    - ECHA 2014a, HSDB 2008a
        - 1,2,4-Trimethylbenzene has a flash point of 44°C in a closed cup test.

  - ToxServices classified 1,2,4-trimethylbenzene as a GHS Category 3 flammable liquid. GHS Category 3 flammable liquids have flash points ≥ 23°C and ≤ 60°C (UN 2013).
- 1,3,5-Trimethylbenzene, CAS #108-67-8
  - ECHA 2014b, HSDB 2008b
    - 1,3,5-Trimethylbenzene has a flash point of 50°C in a closed cup test.
  - ToxServices classified 1,3,5-trimethylbenzene as a GHS Category 3 flammable liquid. GHS Category 3 flammable liquids have flash points ≥ 23°C and ≤ 60°C (UN 2013).

References

Chemical Carcinogenesis Research Information System (CCRIS). 2000. Entry for 1,2,3-Trimethylbenzene (CAS #526-73-8). CCRIS Record Number 8145. Last Revision date March 13, 2000. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/newtoxnet/ccris.htm.

ChemIDplus. 2014a. Entry for 1,2,4-Trimethylbenzene (CAS #95-63-6). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/rn/95-63-6.

ChemIDplus. 2014b. Entry for 1,3,5-Trimethylbenzene (CAS #108-67-8). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/rn/108-67-8.

ChemIDplus. 2014c. Entry for 1,2,3-Trimethylbenzene (CAS #526-73-8). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/rn/526-73-8.

ChemIDplus. 2014d. Entry for Trimethylbenzenes (CAS #25551-13-7). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/rn/25551-13-7.

ChemIDplus. 2014e. Entry for Aromatic Naphtha, Type I (CAS #64742-95-6). United States National Library of Medicine. Available: http://chem.sis.nlm.nih.gov/chemidplus/rn/64742-95-6.

Clean Production Action (CPA). 2011. The GreenScreen® for Safer Chemicals Version 1.2 Benchmarks. Dated October 2011. Available: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2012a. The GreenScreen® for Safer Chemicals Version 1.2 Criteria. Dated: November 2012. Available: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2012b. List Translator. Dated February 2012. Available: http://www.greenscreenchemicals.org/.

Clean Production Action (CPA). 2013. The GreenScreen® for Safer Chemicals Chemical Hazard Assessment Procedure. Version 1.2 Guidance. Dated August 31, 2013. Available: http://www.greenscreenchemicals.org/.

European Chemicals Agency (ECHA). 2014a. REACH Dossier for 1,2,4-Trimethylbenzene (CAS #95-63-6). Available: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d8c70d0-3262-58fd-e044-00144f67d249/DISS-9d8c70d0-3262-58fd-e044-00144f67d249_DISS-9d8c70d0-3262-58fd-e044-00144f67d249.html.

European Chemicals Agency (ECHA). 2014b. REACH Dossier for Mesitylene (CAS #108-67-8). Available: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c7d981e-7a3d-5b36-e044-00144f67d249/DISS-9c7d981e-7a3d-5b36-e044-00144f67d249_DISS-9c7d981e-7a3d-5b36-e044-00144f67d249.html.

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

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

Hazardous Substances Data Bank (HSDB). 2008a. Entry for 1,2,4-Trimethylbenzene (CAS #95-63-6). HSDB Number 5293. Last revision data April 14, 2008. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

Hazardous Substances Data Bank (HSDB). 2008b. Entry for 1,3,5-Trimethylbenzene (CAS #108-67-8). HSDB Number 92. Last revision data April 14, 2008. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

Hazardous Substances Data Bank (HSDB). 2008c. Entry for 1,2,3-Trimethylbenzene (CAS #526-73-8). HSDB Number 7551. Last revision data April 14, 2008. United States National Library of Medicine. Available: http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

Pharos. 2014. Pharos Chemical and Material Library Entry for 1,2,4-Trimethylbenzene (CAS #95-63-6). Available: http://www.pharosproject.net/material/.

Sigma-Aldrich. 2014a. Safety Data Sheet for 1,2,4-Trimethylbenzene (CAS #95-63-6). Product Number T73601. Version 4.4. Revision date July 2, 2014. Available: http://www.sigmaaldrich.com/catalog/product/aldrich/t73601?lang=en&region=US

Sigma-Aldrich. 2014b. Safety Data Sheet for Mesitylene (CAS #108-67-8). Product Number M7200. Version 3.9. Revision date July 18, 2014. Available: http://www.sigmaaldrich.com/catalog/product/sial/m7200?lang=en&region=US.

Sigma-Aldrich. 2014c. Safety Data Sheet for 1,2,3-Trimethylbenzene (CAS #526-73-8). Product Number T73202. Version 5.1. Revision date July 8, 2014. Available: http://www.sigmaaldrich.com/catalog/product/aldrich/t73202?lang=en&region=US.

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

ToxTree. 2013. Estimation of Toxic Hazard- A Decision Tree Approach v2.6.0. Available: http://toxtree.sourceforge.net.

United Nations (UN). 2013. Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Fifth Revised Edition. ST/SG/AC/10/30/Rev.5. Available: http://www.unece.org/trans/danger/publi/ghs/ghs_rev05/05files_e.html.

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). 2012. 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). 2013. Toxicological Review of Trimethylbenzenes (CASRN 25551-13-7, 95-63-6, 526-73-8, and 108-67-8) In Support of Summary Information on the Integrated Risk Information System (IRIS). Revised External Review Draft.

EPA/635/R-13/171a. Dated August 2013. National Center for Environmental Assessment, Office of Research and Development. Available:
http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=254525

APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Trimethylbenzenes (CAS #95-63-6, 108-67-8, 526-73-6, 25551-13-7)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	**Trimethylbenzenes**	**95-63-6, 108-67-8, 526-73-6, 25551-13-7**	*L*	**M**	*M*	**L**	DG	**M**	**M**	**L**	**vH**	**H**	**L**	DG	**H**	**H**	**H**	**H**	*H*	**L**	*L*	**M**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Trimethylbenzenes	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Trimethylbenzenes	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 1,2,4-Trimethylbenzene (CAS #95-63-6)

1,2,4-Trimethylbenzene

CAS RN: 95-63-6

Synonyms: Pseudocumene

Detailed Direct Hazard Listings — Quickscreen

ACUTE AQUATIC	Japan METI/MOE - GHS Classifications (GHS-Japan) Hazardous to the aquatic environment (acute) - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H411 - Aquatic Chronic 2 - Toxic to aquatic life with long lasting effects - GreenScreen Benchmark Possible 1 (LT-P1) - occupational hazard only - HPD
CHRON AQUATIC	Japan METI/MOE - GHS Classifications (GHS-Japan) Hazardous to the aquatic environment (chronic) - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
DEVELOPMENTAL	German MAK - List of Substances (MAK) Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
RESPIRATORY	EC - Risk Phrases (EU R-Phrases) R37: Irritating to respiratory system. - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	EC - Risk Phrases (EU R-Phrases) R20: Harmful by inhalation. - GreenScreen Benchmark Unspecified (LT-U) - HPD
MAMMALIAN	EC - CLP/GHS Hazard Statements (EU H-Statements) H332 Harmful if inhaled - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (inhalation) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following repeated exposure - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following single exposure - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	EC - Risk Phrases (EU R-Phrases) R36: Irritating to eyes. - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H319 Causes serious eye irritation - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	EC - Risk Phrases (EU R-Phrases) R38: Irritating to skin. - GreenScreen Benchmark Unspecified (LT-U) - HPD
SKIN IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H315 Causes skin irritation - GreenScreen Benchmark Unspecified (LT-U) - HPD
SKIN IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.3B - Mildly irritating to the skin - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	EC - CLP/GHS Hazard Statements (EU H-Statements) H335 May cause respiratory irritation - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	New Zealand HSNO/GHS (GHS-New Zealand) 6.9B (inhalation) - Harmful to human target organs or systems - GreenScreen Benchmark Unspecified (LT-U)

ACUTE AQUATIC	**EC - Risk Phrases (EU R-Phrases)** R51: Toxic to aquatic organisms. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only - HPD
CHRON AQUATIC	**EC - Risk Phrases (EU R-Phrases)** R53: May cause long-term adverse effects in the aquatic environment. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
CHRON AQUATIC	**New Zealand HSNO/GHS (GHS-New Zealand)** 9.1B (crustacean) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	**New Zealand HSNO/GHS (GHS-New Zealand)** 9.1B (fish) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	**EC - CLP/GHS Hazard Statements (EU H-Statements)** H226 Flammable liquid and vapour - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
FLAMMABLE	**Québec CSST - WHMIS Classifications (WHMIS)** Class B3 - Combustible liquids - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	**New Zealand HSNO/GHS (GHS-New Zealand)** 3.1C - Flammable Liquids: medium hazard - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	**Japan METI/MOE - GHS Classifications (GHS-Japan)** Flammable liquids - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	**New Zealand HSNO/GHS (GHS-New Zealand)** 6.1E (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	**Japan METI/MOE - GHS Classifications (GHS-Japan)** Aspiration hazard - Category 1 - Not included in GreenScreen - occupational hazard only
FLAMMABLE	**EC - Risk Phrases (EU R-Phrases)** R10: Flammable LIQUID - Not included in GreenScreen
RESTRICTED LIST	**German FEA - Substances Hazardous to Waters (VwVwS)** Class 2 Hazard to Waters - GreenScreen Benchmark Possible 1 (LT-P1) - HPD

Compound Group Hazard Listings

DEVELOPMENTAL	**German MAK - List of Substances (MAK)** Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
RESTRICTED LIST	**CA SCP Candidate Chemicals** Full Candidate Chemical List - Not included in GreenScreen

APPENDIX D: Pharos Output for 1,3,5-Trimethylbenzene (CAS #108-67-8)

MESITYLENE

CAS RN: 108-67-8

Synonyms: 1,3,5-Trimethylbenzene; 3,5-Dimethyltoluene

Detailed Direct Hazard Listings — Quickscreen

ACUTE AQUATIC	Japan METI/MOE - GHS Classifications (GHS-Japan) Hazardous to the aquatic environment (acute) - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H411 - Aquatic Chronic 2 - Toxic to aquatic life with long lasting effects - GreenScreen Benchmark Possible 1 (LT-P1) - occupational hazard only - HPD
CHRON AQUATIC	Japan METI/MOE - GHS Classifications (GHS-Japan) Hazardous to the aquatic environment (chronic) - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
DEVELOPMENTAL	German MAK - List of Substances (MAK) Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
RESPIRATORY	EC - Risk Phrases (EU R-Phrases) R37: Irritating to respiratory system. - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following single exposure - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	Japan METI/MOE - GHS Classifications (GHS-Japan) Serious eye damage / eye irritation - Category 2B - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.3B - Mildly irritating to the skin - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	Japan METI/MOE - GHS Classifications (GHS-Japan) Skin corrosion / irritation - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	EC - CLP/GHS Hazard Statements (EU H-Statements) H335 May cause respiratory irritation - GreenScreen Benchmark Unspecified (LT-U)
ACUTE AQUATIC	EC - Risk Phrases (EU R-Phrases) R51: Toxic to aquatic organisms. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only - HPD
CHRON AQUATIC	EC - Risk Phrases (EU R-Phrases) R53: May cause long-term adverse effects in the aquatic environment. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
CHRON AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1B (crustacean) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1C (algal) - Harmful in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1C (fish) - Harmful in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	EC - CLP/GHS Hazard Statements (EU H-Statements) H226 Flammable liquid and vapour - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
FLAMMABLE	Québec CSST - WHMIS Classifications (WHMIS) Class B3 - Combustible liquids - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	New Zealand HSNO/GHS (GHS-New Zealand) 3.1C - Flammable Liquids: medium hazard - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	Japan METI/MOE - GHS Classifications (GHS-Japan) Flammable liquids - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Aspiration hazard - Category 1 - Not included in GreenScreen - occupational hazard only
FLAMMABLE	EC - Risk Phrases (EU R-Phrases) R10: Flammable LIQUID - Not included in GreenScreen

Compound Group Hazard Listings

DEVELOPMENTAL	German MAK - List of Substances (MAK) Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
RESTRICTED LIST	CA SCP Candidate Chemicals Full Candidate Chemical List - Not included in GreenScreen

APPENDIX E: Pharos Output for 1,2,3-Trimethylbenzene (CAS #526-73-8)

1,2,3-trimethylbenzene

CAS RN: 526-73-8

Direct Chemical and Compound Hazard Quickscreen — Detailed Hazard Listings

Medium Hazard of...

DEVELOPMENTAL — German MAK - List of Substances (MAK): Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)

FLAMMABLE — Québec CSST - WHMIS Classifications (WHMIS): Class B3 - Combustible liquids - GreenScreen Benchmark Unspecified (LT-U) {and 1 other}

Potential concern...

MAMMALIAN — New Zealand HSNO/GHS (GHS-New Zealand): 6.1E (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)

This chemical is NOT present on the hazard lists scanned for the following health and ecotoxicity endpoints...

PBT	CANCER	REPRODUCTIVE	ENDOCRINE	GENE MUTATION
RESPIRATORY	NEUROTOXICITY	EYE IRRITATION	SKIN IRRITATION	SKIN SENSITIZE
ORGAN TOXICANT	ACUTE AQUATIC	CHRON AQUATIC	TERRESTRIAL	REACTIVE
GLOBAL WARMING	OZONE DEPLETION	RESTRICTED LIST		

APPENDIX F: Pharos Output for Trimethylbenzenes (CAS #25551-13-7)

Search Results for '25551-13-7 '

Companies (0) | Building Products (0) | Chemicals, Compounds, and Biobased Materials (0) | Signal Articles (0) | Certifications (0)

Companies

*There were no companies found that match the search term **25551-13-7** .*

Back to top

Building Products

*There were no products found that match the search term **25551-13-7** .*

Back to top

Chemicals, Compounds, and Biobased Materials

*There were no chemicals, compounds, or biobased materials found that match the search term **25551-13-7** .*

Back to top

Signal Articles

*There were no Signal articles found that match the search term **25551-13-7** .*

Back to top

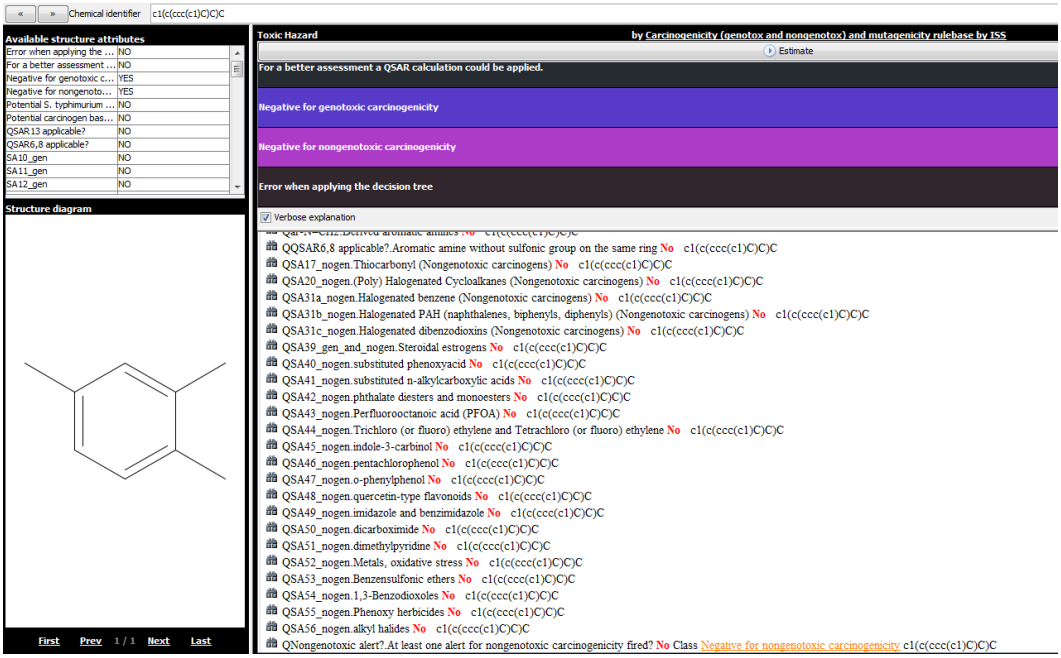
Certifications

*There were no certifications found that match the search term **25551-13-7** .*

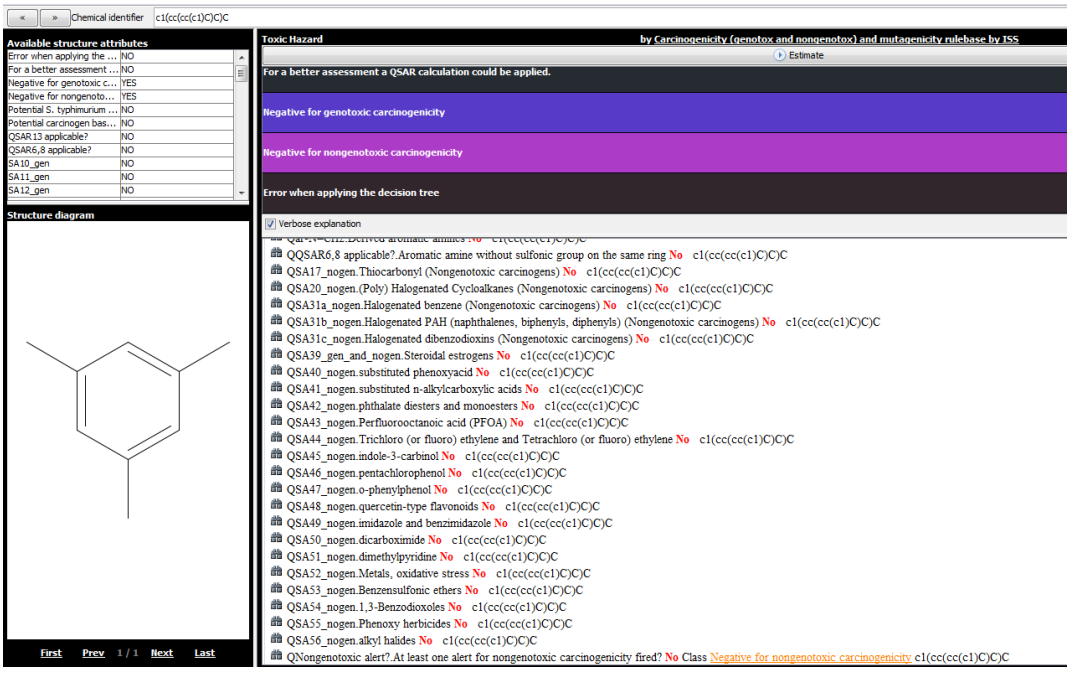
Back to top

APPENDIX G: ToxTree Carcinogenicity Results for Trimethylbenzenes

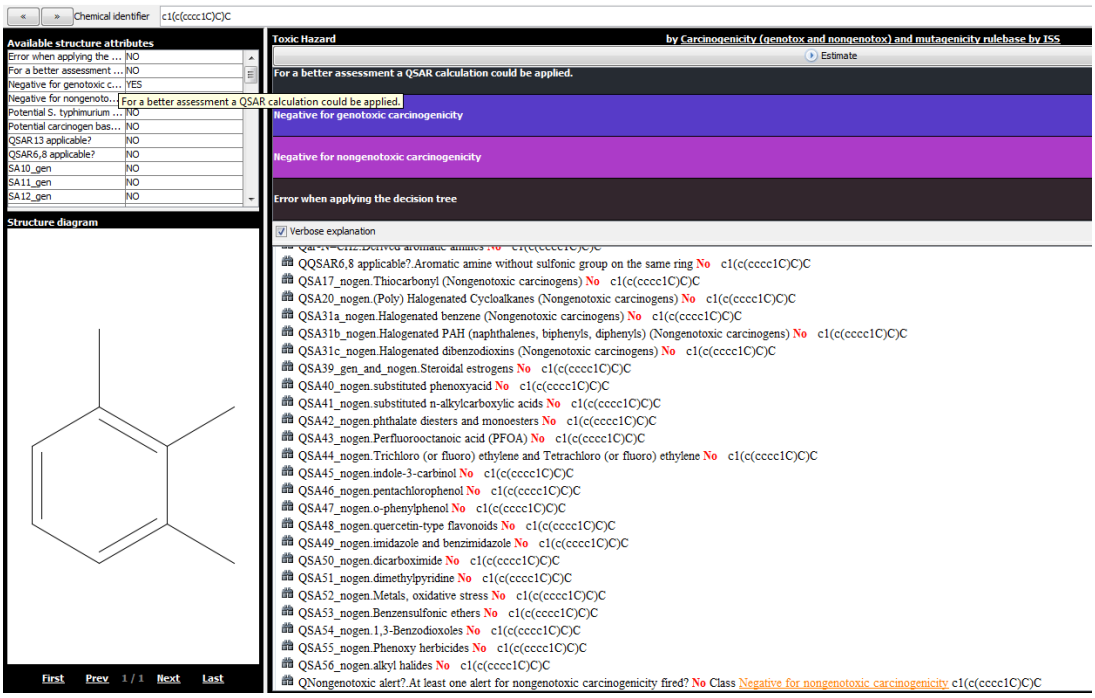
1,2,4-Trimethylbenzene, CAS #95-63-6 – Negative for genotoxic and non-genotoxic carcinogenicity



1,3,5-Trimethylbenzene, CAS #108-67-8 – Negative for genotoxic and non-genotoxic carcinogenicity



1,2,3-Trimethylbenzene, CAS #526-73-8 – Negative for genotoxic and non-genotoxic carcinogenicity



APPENDIX H: EPISuite Modeling Results for Trimethylbenzenes (CAS #95-63-6, 108-67-8, 526-73-6, 25551-13-7)

1,2,4-Trimethylbenzene, CAS #95-63-6 -

CAS Number: 95-63-6
SMILES: c(ccc(c1C)C)(c1)C
CHEM: Benzene, 1,2,4-trimethyl-
MOL FOR: C9 H12
MOL WT: 120.20
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log K_{ow} (octanol-water): 3.65
Boiling Point (deg C): ------
Melting Point (deg C): -43.77
Vapor Pressure (mm Hg): 2.25
Water Solubility (mg/L): 57
Henry LC (atm-m^3/mole): ------

Log Octanol-Water Partition Coef (SRC):
Log K_{ow} (K_{ow}WIN v1.68 estimate) = 3.63
Log K_{ow} (Exper. database match) = 3.63
Exper. Ref: HANSCH, C. ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 169.97 (Adapted Stein & Brown method)
Melting Pt (deg C): -22.46 (Mean or Weighted MP)
VP (mm Hg,25 deg C): 1.62 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 215 (Mean VP of Antoine & Grain methods)
MP (exp database): -43.8 deg C
BP (exp database): 169.3 deg C
VP (exp database): 2.10E+00 mm Hg (2.80E+002 Pa) at 25 deg C

Water Solubility Estimate from Log K_{ow} (WSK_{ow} v1.42):
Water Solubility at 25 deg C (mg/L): 77.89
log K_{ow} used: 3.65 (user entered)
melt pt used: -43.77 deg C
Water Sol (Exper. database match) = 57 mg/L (25 deg C)
Exper. Ref: MCAULIFFE, C. (1966)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 54.682 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 7.24E-003 atm-m^3/mole (7.34E+002 Pa-m^3/mole)

Group Method: 6.58E-003 atm-m^3/mole (6.67E+002 Pa-m^3/mole)
Exper Database: 6.16E-03 atm-m^3/mole (6.24E+002 Pa-m^3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 6.243E-003 atm-m3/mole (6.326E+002 Pa-m^3/mole)
VP: 2.25 mm Hg (source: User-Entered)
WS: 57 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Log K_{ow} used: 3.65 (user entered)
Log K_{aw} used: -0.599 (exp database)
Log K_{oa} (K_{oa}WIN v1.10 estimate): 4.249
Log K_{oa} (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.8543
Biowin2 (Non-Linear Model): 0.9541
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.7090 (weeks-months)
Biowin4 (Primary Survey Model): 3.4687 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.5036
Biowin6 (MITI Non-Linear Model): 0.5837
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): -0.5655
Ready Biodegradability Prediction: NO

Hydrocarbon Biodegradation (BioHCwin v1.01):
LOG BioHC Half-Life (days): 0.6425
BioHC Half-Life (days): 4.3899

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 300 Pa (2.25 mm Hg)
Log K_{oa} (K_{oa}win est): 4.249
Kp (particle/gas partition coef. (m^3/ug)):
Mackay model: 1E-008
Octanol/air (K_{oa}) model: 4.36E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 3.61E-007
Mackay model: 8E-007
Octanol/air (K_{oa}) model: 3.48E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 16.6980 E-12 cm^3/molecule-sec
Half-Life = 0.641 Days (12-hr. day; 1.5E6 OH/cm^3)
Half-Life = 7.687 Hrs.
Ozone Reaction:

No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
5.81E-007 (Junge-Pankow, Mackay avg)
3.48E-007 (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 614.3 L/kg (MCI method)
Log K_{oc}: 2.788 (MCI method)
K_{oc}: 1470 L/kg (K_{ow} method)
Log K_{oc}: 3.167 (K_{ow} method)

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

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 2.075 (BCF = 118.9 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -0.0794 days (HL = 0.8329 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.158 (BCF = 143.8)
Log BAF Arnot-Gobas method (upper trophic) = 2.158 (BAF = 143.8)
log K_{ow} used: 3.65 (user entered)

Volatilization from Water:
Henry LC: 0.00616 atm-m^3/mole (Henry experimental database)
Half-Life from Model River: 1.223 hours
Half-Life from Model Lake: 105.3 hours (4.386 days)

Removal In Wastewater Treatment:
Total removal: 73.68 percent
Total biodegradation: 0.10 percent
Total sludge adsorption: 11.55 percent
Total to Air: 62.03 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr.)	Emissions (kg/hr.)
Air	3.22	7.9	1000
Water	31.9	900	1000
Soil	63.8	1.8e+003	1000
Sediment	1.08	8.1e+003	0

Persistence Time: 253 hr.

1,3,5-Trimethylbenzene, CAS #108-67-8

CAS Number: 108-67-8
SMILES: c(cc(cc1C)C)(c1)C
CHEM: Benzene, 1,3,5-trimethyl-
MOL FOR: C9 H12
MOL WT: 120.20
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log K_{ow} (octanol-water): 3.84
Boiling Point (deg C): ------
Melting Point (deg C): -44.70
Vapor Pressure (mm Hg): 2.48
Water Solubility (mg/L): 48.2
Henry LC (atm-m^3/mole): ------

Log Octanol-Water Partition Coef (SRC):
Log K_{ow} (K_{ow}WIN v1.68 estimate) = 3.63
Log K_{ow} (Exper. database match) = 3.42
Exper. Ref: HANSCH, C. ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 169.97 (Adapted Stein & Brown method)
Melting Pt (deg C): -22.46 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 2.01 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 268 (Mean VP of Antoine & Grain methods)
MP (exp database): -44.7 deg C
BP (exp database): 164.7 deg C
VP (exp database): 2.10E+00 mm Hg (2.80E+002 Pa) at 25 deg C

Water Solubility Estimate from Log K_{ow} (WSK_{ow} v1.42):
Water Solubility at 25 deg C (mg/L): 51.18
log K_{ow} used: 3.84 (user entered)
melt pt used: -44.70 deg C
Water Sol (Exper. database match) = 48.2 mg/L (25 deg C)
Exper. Ref: YALKOWSKY, S.H. & HE,Y (2003)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 54.682 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 7.24E-003 atm-m^3/mole (7.34E+002 Pa-m^3/mole)
Group Method: 6.58E-003 atm-m^3/mole (6.67E+002 Pa-m^3/mole)
Exper Database: 8.77E-03 atm-m^3/mole (8.89E+002 Pa-m^3/mole)
For Henry LC Comparison Purposes:

User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 8.138E-003 atm-m^3/mole (8.245E+002 Pa-m^3/mole)
VP: 2.48 mm Hg (source: User-Entered)
WS: 48.2 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Log K_{ow} used: 3.84 (user entered)
Log K_{aw} used: -0.445 (exp database)
Log K_{oa} (K_{oa}WIN v1.10 estimate): 4.285
Log K_{oa} (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.8543
Biowin2 (Non-Linear Model): 0.9541
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.7090 (weeks-months)
Biowin4 (Primary Survey Model): 3.4687 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.5036
Biowin6 (MITI Non-Linear Model): 0.5837
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): -0.5655
Ready Biodegradability Prediction: NO

Hydrocarbon Biodegradation (BioHCwin v1.01):
LOG BioHC Half-Life (days): 0.6425
BioHC Half-Life (days): 4.3899

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 331 Pa (2.48 mm Hg)
Log K_{oa} (K_{oa}win est): 4.285
Kp (particle/gas partition coef. (m^3/ug)):
Mackay model: 9.07E-009
Octanol/air (K_{oa}) model: 4.73E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 3.28E-007
Mackay model: 7.26E-007
Octanol/air (K_{oa}) model: 3.79E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 35.0993 E-12 cm^3/molecule-sec
Half-Life = 0.305 Days (12-hr day; 1.5E6 OH/cm^3)
Half-Life = 3.657 Hrs.
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
5.27E-007 (Junge-Pankow, Mackay avg)

3.79E-007 (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 602.1 L/kg (MCI method)
Log K_{oc}: 2.780 (MCI method)
K_{oc}: 2149 L/kg (K_{ow} method)
Log K_{oc}: 3.332 (K_{ow} method)
Experimental Log K_{oc}: 2.82 (database)

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 = 2.201 (BCF = 158.7 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -0.0210 days (HL = 0.9528 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.632 (BCF = 428.6)
Log BAF Arnot-Gobas method (upper trophic) = 2.633 (BAF = 429.6)
log K_{ow} used: 3.84 (user entered)

Volatilization from Water:
Henry LC: 0.00877 atm-m^3/mole (Henry experimental database)
Half-Life from Model River: 1.192 hours
Half-Life from Model Lake: 104.9 hours (4.372 days)

Removal In Wastewater Treatment:
Total removal: 80.41 percent
Total biodegradation: 0.11 percent
Total sludge adsorption: 15.58 percent
Total to Air: 64.73 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr.)	Emissions (kg/hr.)
Air	2.39	4.46	1000
Water	38.8	900	1000
Soil	57.5	1.8e+003	1000
Sediment	1.29	8.1e+003	0

Persistence Time: 206 hr.

1,2,3-Trimethylbenzene, CAS #526-73-8

CAS Number: 526-73-8
SMILES: c(c(c(cc1)C)C)(c1)C
CHEM: Benzene, 1,2,3-trimethyl-
MOL FOR: C9 H12
MOL WT: 120.20
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log K_{ow} (octanol-water): 3.66
Boiling Point (deg C): ------
Melting Point (deg C): -25.40
Vapor Pressure (mm Hg): 1.69
Water Solubility (mg/L): 75.2
Henry LC (atm-m^3/mole): ------

Log Octanol-Water Partition Coef (SRC):
Log K_{ow} (K_{ow}WIN v1.68 estimate) = 3.63
Log K_{ow} (Exper. database match) = 3.66
Exper. Ref: HANSCH, C. ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 169.97 (Adapted Stein & Brown method)
Melting Pt (deg C): -22.46 (Mean or Weighted MP)
VP (mm Hg,25 deg C): 1.17 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 155 (Mean VP of Antoine & Grain methods)
MP (exp database): -25.4 deg C
BP (exp database): 176.1 deg C
VP (exp database): 1.69E+00 mm Hg (2.25E+002 Pa) at 25 deg C

Water Solubility Estimate from Log K_{ow} (WSK_{ow} v1.42):
Water Solubility at 25 deg C (mg/L): 76.19
log K_{ow} used: 3.66 (user entered)
melt pt used: -25.40 deg C
Water Sol (Exper. database match) = 75.2 mg/L (25 deg C)
Exper. Ref: YALKOWSKY, S.H. & DANNENFELSER, R.M. (1992)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 54.682 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 7.24E-003 atm-m^3/mole (7.34E+002 Pa-m^3/mole)
Group Method: 6.58E-003 atm-m^3/mole (6.67E+002 Pa-m^3/mole)
Exper Database: 4.36E-03 atm-m^3/mole (4.42E+002 Pa-m^3/mole)
For Henry LC Comparison Purposes:

User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 3.554E-003 atm-m^3/mole (3.601E+002 Pa-m^3/mole)
VP: 1.69 mm Hg (source: User-Entered)
WS: 75.2 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Log K_{ow} used: 3.66 (user entered)
Log K_{aw} used: -0.749 (exp database)
Log K_{oa} (K_{oa}WIN v1.10 estimate): 4.409
Log K_{oa} (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.8543
Biowin2 (Non-Linear Model): 0.9541
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.7090 (weeks-months)
Biowin4 (Primary Survey Model): 3.4687 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.5036
Biowin6 (MITI Non-Linear Model): 0.5837
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): -0.5655
Ready Biodegradability Prediction: NO

Hydrocarbon Biodegradation (BioHCwin v1.01):
LOG BioHC Half-Life (days): 0.6425
BioHC Half-Life (days): 4.3899

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 225 Pa (1.69 mm Hg)
Log K_{oa} (K_{oa}win est): 4.409
Kp (particle/gas partition coef. (m^3/ug)):
Mackay model: 1.33E-008
Octanol/air (K_{oa}) model: 6.3E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 4.81E-007
Mackay model: 1.07E-006
Octanol/air (K_{oa}) model: 5.04E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 16.6980 E-12 cm^3/molecule-sec
Half-Life = 0.641 Days (12-hr day; 1.5E6 OH/cm^3)
Half-Life = 7.687 Hrs.
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
7.73E-007 (Junge-Pankow, Mackay avg)

5.04E-007 (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 626.9 L/kg (MCI method)
Log K_{oc}: 2.797 (MCI method)
K_{oc}: 1500 L/kg (K_{ow} method)
Log K_{oc}: 3.176 (K_{ow} method)
Experimental Log K_{oc}: 2.8 (database)

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 = 2.082 (BCF = 120.7 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -0.0763 days (HL = 0.8388 days)
Log BCF Arnot-Gobas method (upper trophic) = 2.218 (BCF = 165.3)
Log BAF Arnot-Gobas method (upper trophic) = 2.218 (BAF = 165.4)
log K_{ow} used: 3.66 (user entered)

Volatilization from Water:
Henry LC: 0.00436 atm-m^3/mole (Henry experimental database)
Half-Life from Model River: 1.266 hours
Half-Life from Model Lake: 105.7 hours (4.406 days)

Removal In Wastewater Treatment:
Total removal: 67.34 percent
Total biodegradation: 0.11 percent
Total sludge adsorption: 12.35 percent
Total to Air: 54.88 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr.)	Emissions (kg/hr.)
Air	2.57	7.85	1000
Water	26.6	900	1000
Soil	69.9	1.8e+003	1000
Sediment	0.921	8.1e+003	0

Persistence Time: 306 hr.

Sources to Check for GreenScreen® Hazard Assessment

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

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

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

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

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

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

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

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

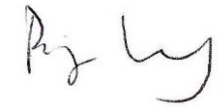
European Chemicals Agency (ECHA) REACH Dossiers: http://echa.europa.eu/

Licensed GreenScreen® Profilers

Trimethylbenzenes GreenScreen® Evaluation Prepared by:

Zach Guerrette, Ph.D.
Toxicologist
ToxServices LLC

Trimethylbenzenes GreenScreen® Evaluation QC'd by:



Bingxuan Wang, Ph.D.
Toxicologist
ToxServices LLC