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Trimethoxy(methyl)silane (CAS# 1185-55-3) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

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December 1, 2014

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GreenScreen® Executive Summary for Trimethoxy(methyl)silane (CAS #1185-55-3)

Trimethoxy(methyl)silane is a chemical that functions as a monomer in the production of silicone polymers or resins, as a chemical intermediate in the production of other organosilicon substances, in coatings to provide bonding or adhesion, in sealants as a cross-linking agent and adhesion promoter, and in electronics, textiles, and laboratory applications.

Trimethoxy(methyl)silane was assigned a GreenScreen® Benchmark Score of 1_{TP} ("Avoid-Chemical of High Concern due to Transformation Products"). It has Moderate Group I Human Toxicity (mutagenicity-M and endocrine activity-E) and High flammability-F. This corresponds to GreenScreen® benchmark classifications 2e and 2g in CPA 2011. Data gaps (DG) exist for respiratory sensitization-SnR*. As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), trimethoxy(methyl)silane meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. However, the transformation product methanol, which is formed by hydrolysis, is an LT-1 chemical. Therefore the final Benchmark score is reduced to a 1_{TP}. In a worst-case scenario, if trimethoxy(methyl)silane were assigned a High score for the data gap SnR*, it would still 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 1_{TP} ("Avoid-Chemical of High Concern due to Transformation Products") is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for Trimethoxy(methyl)silane

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*	L	L	*M*	L	L	M	M	L	*M*	DG	L	L	L	L	*M*	*vL*	*L*	H

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.

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GreenScreen® Assessment for Trimethoxy(methyl)silane (CAS #1185-55-3)

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

Chemical Name: Trimethoxy(methyl)silane

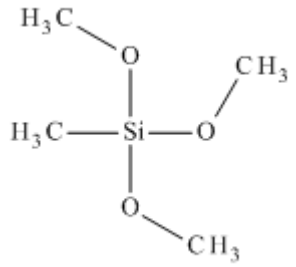
CAS Number: 1185-55-3

GreenScreen® Assessment Prepared By:
Name: Jennifer Rutkiewicz, 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: December 1, 2014

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

Chemical Structure(s):



Also called: Methyltrimethoxysilane; Trimethoxymethylsilane; Silane, methyltrimethoxy-; Silane, trimethoxymethyl- (ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
No surrogates were used in this assessment.

Identify Applications/Functional Uses: (Dow Corning 2012)
1. Monomer in the production of silicone polymers or resins
2. Chemical intermediate in the production of other organosilicon substances
3. Coatings to provide bonding or adhesion
4. Sealants as a cross-linking agent and adhesion promoter
5. Electronics

[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

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6. Textiles
7. Laboratory applications

GreenScreen® Summary Rating for Trimethoxy(methyl)silane[4]: Trimethoxy(methyl)silane was assigned a GreenScreen® Benchmark Score of 1_{TP} ("Avoid-Chemical of High Concern due to Transformation Products"). It has Moderate Group I Human Toxicity (mutagenicity-M and endocrine activity-E) and High flammability-F. This corresponds to GreenScreen® benchmark classifications 2e and 2g in CPA 2011, 2012a. Data gaps (DG) exist for respiratory sensitization-SnR*. As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), trimethoxy(methyl)silane meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. However, the transformation product methanol, which is formed by hydrolysis, is an LT-1 chemical. Therefore the final Benchmark score is reduced to a 1_{TP}. In a worst-case scenario, if trimethoxy(methyl)silane were assigned a High score for the data gap SnR*, it would still be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Trimethoxy(methyl)silane

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*	**L**	**L**	*M*	**L**	**L**	**M**	**M**	**L**	*M*	DG	**L**	**L**	**L**	**L**	*M*	*vL*	*L*	**H**

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]

Trimethoxy(methyl)silane undergoes rapid hydrolysis in the environment, producing methanol (3 moles) and methylsilanetriol (1 mole) (ECHA 2014). Methanol is readily biodegradable in the environment. Therefore, methanol is likely to be rapidly released after the hydrolysis of the parent compound and then rapidly degraded, reducing the potential for human/environmental exposure. However, as a conservative approach, ToxServices considered methanol a feasible and relevant transformation product and used the LT-1 score for methanol to reduce the Benchmark score of the parent compound.

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

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

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Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	Feasible and Relevant?	GreenScreen® List Translator Score or Benchmark Score [6,7]
Unknown	Unknown	Hydrolysis	Methylsilanetriol	2445-53-6	Y	LT-U
Unknown	Unknown	Hydrolysis	Methanol	67-56-1	Y	LT-1

Introduction

Trimethoxy(methyl)silane is an organic silicon compound that is used as a monomer in the production of silicone polymers or resins, as a chemical intermediate in the production of other organosilicon substances, in coatings to provide bonding or adhesion, in sealants as a cross-linking agent and adhesion promoter, and in electronics, textiles, and laboratory applications (Dow Corning 2012).

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

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 trimethoxy(methyl)silane can be found in Appendix C and a summary of the results can be found below:

Skin Irritation

New Zealand HSNO/GHS (GHS-New Zealand) 6.3B - Mildly irritating to the skin (Category 3)

Eye Irritation

New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye (Category 2A)

Persistence

Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent

Flammability

New Zealand HSNO/GHS (GHS-New Zealand) 3.1B - Flammable Liquids: high hazard (Category 2)

When appropriate, the equivalent GHS hazard classifications were identified for GHS New Zealand classifications (EPA 2012)

[6] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the lists in the List Translator electronically.

[7] The way you conduct assessments for transformation products depends on the Benchmark Score of the parent chemical (See Guidance).

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PhysicoChemical Properties of Trimethoxy(methyl)silane

Trimethoxy(methyl)silane is a liquid at room temperature. Its high vapor pressure of 22.4 mmHg indicates that it is likely to form a gas. It is highly soluble in water (> 10,000 mg/L) and its estimated log K_{ow} of -0.67 indicates that it is not expected to bioaccumulate.

Table 1: Physical and Chemical Properties of Trimethoxy(methyl)silane (CAS #1185-55-3)

Property	Value	Reference
Molecular formula	C4-H12-O3-Si	ChemIDplus 2014
SMILES Notation	[Si](OC)(OC)(OC)C	ChemIDplus 2014
Molecular weight	136.222	ChemIDplus 2014
Physical state	Liquid	ECHA 2014
Appearance	Clear, colorless	ECHA 2014
Melting point	< -77°C	ECHA 2014
Vapor pressure	2,990 Pa (22.4 mmHg) at 20°C	ECHA 2014
Water solubility	> 10,000 mg/L (hydrolysis product)	ECHA 2014
Dissociation constant	Not identified	
Density/specific gravity	0.95 g/cm^3 at 25°C	ECHA 2014
Partition coefficient	log K_{ow} = -0.67 (est.)	U.S. EPA 2012

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

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

Trimethoxy(methyl)silane was assigned a score of Low for carcinogenicity based on negative modeling results. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and are negative for carcinogenicity, and the chemical is not present on authoritative or screening lists (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- U.S. EPA 2012.
  - OncoLogic predicts that silicon compounds are of marginal concern for carcinogenicity. See Appendix D for justification.
- ToxTree 2013
  - Trimethoxy(methyl)silane was predicted to be negative for both genotoxic carcinogenicity and nongenotoxic carcinogenicity using the ToxTree model using decision tree methodology. See Appendix E for justification.
- Based on the weight of evidence, a score of Low was assigned. OncoLogic predicts that silicon compounds are of marginal concern for carcinogenicity, and ToxTree predicts that trimethoxy(methyl)silane is not a genotoxic or nongenotoxic carcinogen. Confidence in this score is reduced because it is based on modeling.

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

Trimethoxy(methyl)silane was assigned a score of Moderate for mutagenicity/genotoxicity based on positive results in a GLP-compliant *in vitro* mammalian cell mutagenicity assay. GreenScreen® criteria

classify chemicals as a Moderate hazard for mutagenicity/genotoxicity when there is limited or marginal evidence of genotoxicity (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- ECHA 2014
    - Trimethoxy(methyl)silane (purity not specified) was negative in a GLP-compliant Ames reverse mutation assay according to OECD Guideline 471 in *S. typhimurium* strains TA1535, TA1537, TA98, and TA100, and *E. coli* WP2 uvrA when tested at concentrations of 100, 333, 1000, 3333 and 5000 µg/plate with and without metabolic activation. No increase in revertants was seen in any strain at any dose.
    - In a GLP-compliant *in vitro* mammalian cell chromosome aberration test according to OECD Guideline 473 in Chinese hamster ovary (CHO-K1) cells, cells were treated with trimethoxy(methyl)silane at concentration of 170.3, 340.6, 681.2 and 1362.4 µg/ml with and without metabolic activation. No cytotoxicity was observed. A statistically significant dose-dependent increase in structural aberrations was seen with, but not without, metabolic activation. Authors concluded that trimethoxy(methyl)silane was positive with metabolic activation and negative without metabolic activation.
    - In a GLP-compliant *in vitro* mammalian cell mutagenicity assay according to OECD Guideline 476 in mouse lymphoma L5178Y cells, cells were treated with 13 to 1360 µg/ml trimethoxy(methyl)silane (purity not specified) with and without metabolic activation. No cytotoxicity was observed. A statistically significant dose-dependent increase in mutant frequency was seen with metabolic activation. An increase in mutant frequency was seen at the low dose without metabolic activation. Authors concluded that trimethoxy(methyl)silane is positive with metabolic activation and ambiguous without metabolic activation.
    - Trimethoxy(methyl)silane (purity not specified) was negative in a GLP-compliant Ames reverse mutation assay according to OECD Guideline 471 in *S. typhimurium* strains TA1535, TA1537, TA98, and TA100, and *E. coli* WP2 uvrA when tested at concentrations of 62-5000 µg/plate with and without metabolic activation. No increase in revertants was seen in any strain at any dose.
    - Trimethoxy(methyl)silane (purity not specified) was negative in an Ames reverse mutation assay in *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100 when tested at concentrations of 5, 50, 200 and 500 µg/plate with and without metabolic activation.
    - Trimethoxy(methyl)silane (purity not specified) was negative in a GLP-compliant *in vivo* mammalian erythrocyte micronucleus test according to OECD Guideline 474 in male and female CD-1 mice. No increase in micronuclei in the bone marrow of mice (5/sex/dose) was seen 24 or 48 hours after a single oral dose of 0, 500, 1,000, or 2,000 mg/kg trimethoxy(methyl)silane via gavage. Clinical signs (mortality, reduced activity, ataxia and hunched posture) at the mid and high dose suggest systemic availability. Authors concluded that trimethoxy(methyl)silane was negative for clastogenicity *in vivo*.
- Based on the weight of evidence, a score of Moderate was assigned. Negative results in an *in vivo* micronucleus assay were weighed more heavily in the assessment, and indicate that trimethoxy(methyl)silane is not likely to be clastogenic. However, positive results in *in vitro* mammalian cell mutagenicity assays indicate that it may have the potential to be mutagenic. Therefore a score of Moderate was assigned. Confidence in this score is reduced due to conflicting results between bacterial and mammalian cell assays.

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Reproductive Toxicity (R) Score (H, M, or L): L
Trimethoxy(methyl)silane was assigned a score of Low for reproductive toxicity based on a lack of effects on reproductive indices in a GLP-compliant reproductive toxicity screening test in rats. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and are negative for reproductive effects, and the chemical is not present on authoritative or screening lists (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014
  - In a GLP-complaint reproductive and developmental toxicity screening test according to OECD Guideline 422 in Sprague-Dawley rats, animals (10/sex/dose) were administered trimethoxy(methyl)silane (100% purity) at doses of 0, 50, 250, or 1,000 mg/kg/day via gavage for 14 days prior to mating and through a 14 day mating period (males) or postpartum day 3 (females). No effects on reproductive performance (male and female mating index, male and female fertility index, male copulation index, and female conception index) were seen. All females delivered live litters, and there were no effects on litter size. Authors identified a NOAEL of 1,000 mg/kg/day based on the lack of effects on reproduction.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L
Trimethoxy(methyl)silane was assigned a score of Low for developmental toxicity based on a lack of effects on developmental indices in a GLP-compliant developmental toxicity screening test in rats. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data are available and are negative for developmental effects, and the chemical is not present on authoritative or screening lists (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014
  - In the GLP-complaint reproductive and developmental toxicity screening test according to OECD Guideline 422 in Sprague-Dawley rats described above for reproductive toxicity, there were no effects on offspring viability, clinical signs, body weight, or gross pathology. There were no visible external, soft tissue, or skeletal abnormalities. Authors identified a NOAEL of 1,000 mg/kg/day, the highest dose studied, based on the lack of effects on development.

Endocrine Activity (E) Score (H, M, or L): *M*
Trimethoxy(methyl)silane was assigned a score of Moderate for endocrine disruption based on pathological changes to the thyroid gland in a 28-day oral toxicity study in rats. GreenScreen® criteria classify chemicals as a Moderate hazard for endocrine disruption when there is evidence of endocrine activity (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.

- ECHA 2014
    - In the GLP-complaint oral combined repeated dose toxicity study with reproductive and developmental toxicity screening test according to OECD Guideline 422 in Sprague-Dawley rats that is described below for systemic toxicity, thyroid gland follicular cell hyperplasia/hypertrophy was seen in all animals (males and females) at doses of 250 and 1,000 mg/kg/day.
- High Throughput Screening (HTS) Data-
    - HTS data were identified for trimethoxy(methyl)silane using PubChem (http://pubchem.ncbi.nlm.nih.gov/).
    - The data included the following results:
        - Trimethoxy(methyl)silane was active in 0/3 androgen receptor agonist assays and 0/6 androgen receptor antagonist assays.
        - Trimethoxy(methyl)silane was active in 0/3 estrogen receptor-alpha agonist assays and 0/6 estrogen receptor-alpha antagonist assays.
        - Trimethoxy(methyl)silane was active in 0/1 thyroid receptor agonist assay and 0/3 thyroid receptor antagonist assays.
        - The activity of trimethoxy(methyl)silane towards the thyroid stimulating hormone receptor was not evaluated.
- Based on the weight of evidence, a score of Moderate was assigned based on histopathological changes to the thyroid of rats following 28-days of oral exposure to 250 or 1,000 mg/kg/day. Confidence in this score is reduced, as the significance of these changes to hormone regulation was not discussed.

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

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

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

Trimethoxy(methyl)silane was assigned a score of Low for acute toxicity based on an oral LD_{50} of 7,000 mg/kg in mice, dermal LD_{50} of greater than 9,500 mg/kg in rabbits, and inhalation LC_{50} of greater than 42.1 mg/L in rats. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when the most conservative oral and dermal LD_{50} values are greater than 2,000 mg/kg and the most conservative inhalation LC_{50} value is greater than 20 mg/L (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists
    - *Screening:* Not present on any screening lists
- ECHA 2014
    - *Oral*: LD_{50} (rat, male Carworth Farms-Eliss) = 11,685 mg/kg
    - *Oral*: LD_{50} (rat, male Sprague-Dawley) > 9,500 mg/kg
    - *Oral*: LD_{50} (mouse, male and female, strain not specified) = 7,000 mg/kg
    - *Inhalation*: LC_{50} (rat, male and female Sprague-Dawley) > 42.1 mg/L/6h
    - *Inhalation*: LC_{50} (rat, female, strain not specified) > 26,000 ppm/4h (144.9 mg/L/4h[8])
    - *Dermal*: D_{50} (rabbit, sex and strain not specified > 9,500 mg/kg

[8] 26,000 ppm * 136.222 / 24,450 = 144.9 mg/L

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Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose) **(vH, H, M, or L): L**
Trimethoxy(methyl)silane was assigned a score of Low for systemic toxicity (single dose) based on a lack of persistent clinical effects or changes gross organ pathology at doses from 29-9,500 mg/kg in an acute oral toxicity study in rats . GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when no evidence of systemic toxicity is seen below the guidance value of 2,000 mg/kg in an acute oral toxicity study (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014
  - *Oral*: In the acute oral toxicity study in male Carworth Farms-Eliss rats that identified an LD_{50} of 11,685 mg/kg, animals (5/dose) were administered a single oral dose of 8 mL/kg or 16 mL/kg (7,600 or 15,200 g/kg[9]) trimethoxy(methyl)silane (purity not specified) via gavage and were observed for 14 days. Animals were sluggish and demonstrated unsteady gait shortly after dosing. No effects on body weight gain were seen. Congested lungs, mottled livers with prominent acini, and hemorrhage and congestion of the gastrointestinal tract were seen at necropsy.
  - *Oral*: In the acute oral toxicity study in male Sprague-Dawley rats that identified an LD_{50} of > 7,000 mg/kg, animals, animals (5/sex/dose) were administered a single oral dose of 0.031, 0.1, 0.316, 1, 3.16, or 10 mL/kg (29, 95, 300, 950, 3,002, or 9,500 mg/kg[10]) trimethoxy(methyl)silane (purity not specified) via gavage and were observed for an unspecified duration. Depression, labored respiration, ataxia, and excessive urination were seen at the high dose and resolved by day 4. No gross pathological changes were seen at necropsy.
  - *Inhalation*: In the acute inhalation toxicity study in male and female Sprague-Dawley rats that identified an LC_{50}, > 42.1 mg/L/6h, animals (5/sex) were exposed to 42.1 mg/L trimethoxy(methyl)silane (purity not specified) vapor via whole body inhalation for 6 hours and were observed for 14 days. No mortality or effects on body weight were seen. Urinary bladder calculi and kidney foci were seen in both sexes, an enlarged kidney was seen in one male, and abscessed prostate glands were seen in two males.
- Based on the weight of evidence, a score of Low was assigned. The oral toxicity study in Carworth Farms-Eliss rats and inhalation toxicity study in Sprague-Dawley rats are insufficient to assess systemic toxicity, as all doses were greater than the guidance values. As no gross pathological changes were seen in the acute oral toxicity study in Sprague-Dawley rats, which included doses both below and above the guidance value, a score of Low was assigned. Clinical signs(ataxia and depression) will be assessed for neurotoxicity-single dose.

Group II* Score (repeated dose) **(H, M, or L): M**
Trimethoxy(methyl)silane was assigned a score of Moderate for systemic toxicity (repeated dose) based on a LOAEL of 250 mg/kg/day in a 28-day oral toxicity study in rats. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when systemic toxicity is seen between the guidance values of 30 and 300 mg/kg/day (guidance values tripled due to short duration of study) for an oral toxicity study (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists

[9] 8 mL/kg *0.95 g/mL * 1,000 mg/g = 7,600 mg/kg
[10] 0.031 mL/kg *0.95 g/mL * 1,000 mg/g = 29 mg/kg

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  - *Screening:* Not present on any screening lists
- ECHA 2014
  - *Oral*: In the GLP-complaint combined repeated dose toxicity study with reproductive and developmental toxicity screening test according to OECD Guideline 422 in Sprague-Dawley rats that was described previously for reproductive toxicity, the toxicity group animals (10/sex/dose) were administered trimethoxy(methyl)silane (100% purity) at doses of 0, 50, 250, or 1,000 mg/kg/day via gavage for 14 days prior to mating and through a mating for a total treatment period of 28-29 days. Transient inactivity and salivation were observed after dosing. Body weight and weight gain were significantly decreased in males at the high dose. Absolute and relative liver weights were significantly increased in both sexes at the mid and high doses. At the mid and high doses, prothrombin time was significantly increased in males but not females. Platelet concentration was increased in both sexes and red blood cell concentration was increased in males at the high dose. Histopathological changes at the mid and high dose included hepatocellular hypertrophy, periportal vacuolation, ancanthocytosis, thyroid gland hyperplasia/hypertrophy, mucosal lipidosis of the duodenum, and jejunum, and adrenal gland hyperplasia/hypertrophy, apoptosis, and lymphocytic infiltration. Authors identified a NOAEL of 50 mg/kg/day and LOAEL of 250 mg/kg/day. Due to the short duration of the study (28-29 days), these values are compared to tripled guidance values.
  - *Inhalation*: In a subchronic inhalation toxicity study according to OECD Guideline 413 in Crl: CD® (SD) IGS BR VAF/Plus® rats, animals (10/sex/dose) were administered 25, 100, 400, or 1,600 ppm (0.14, 0.56, 2.2, or 8.9 mg/L) trimethoxy(methyl)silane (purity not reported) for 6 hours/day, 5 days/week via whole body inhalation for 90 days. To treatment related changes were seen at up to 0.56 mg/L. At the 2.2 mg/L dose, calculi were seen in the urinary bladder of 2 males, and urinary bladder epithelial hyperplasia was seen in both sexes. Absolute adrenal gland weight was increased by 18% in females. Calculi were also seen in the urinary bladder of 4 males and 1 female at the high dose, and persisted through a 28-day recovery period. Moderate dilation of the kidney was also observed. In females at the high dose, absolute and relative adrenal weights were significantly increased by 25% and 27%, respectively, and relative kidney weights were significantly increased by 12%. Authors identified a NOAEC of 0.56 mg/L and LOAEC of 2.2 mg/L based on effects on the bladder and kidney. These values are equivalent to 0.4 and 1.6 mg/L[11] for a 7 days/week exposure.
- Based on the weight of evidence, a score of Moderate was assigned. The guidance values are tripled for the oral toxicity study due to the 28-day duration of treatment. Therefore the LOAEL of 250 mg/kg/day falls between the tripled guidance values of >30-300 mg/kg/day for a score of Moderate. The NOAEC and LOAEC of 0.4 and 1.6 mg/L for the inhalation toxicity study correspond to a score of Low (>1.0 mg/L) to Moderate (>0.2-1.0 mg/L) via inhalation, but dose spacing is insufficient to determine if effects were seen below the guidance value of 1.0 mg/L. Therefore the score of Moderate was assigned based on the oral toxicity study.

Neurotoxicity (N)
***Group II Score (single dose)* (vH, H, M, or L): M**
Trimethoxy(methyl)silane was assigned a score of Moderate for neurotoxicity (single dose) based on transient neurological effects in acute oral toxicity studies in rats and mice, and in acute inhalation toxicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when available data indicate that GHS Category 3 classification for transient narcotic effects is warranted (CPA 2012a).

[11] 0.56 * 5 days/7 days = 0.4 mg/L

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- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- ECHA 2014
  - *Oral*: In the acute oral toxicity study in male Carworth Farms-Eliss rats that identified an LD_{50} 11,685 mg/kg described above for systemic toxicity, animals (5/dose) were administered a single oral dose of 8 mL/kg or 16 mL/kg (7.6 or 15.2 g/kg) via gavage and were observed for 14 days. Animals were sluggish and demonstrated unsteady gait shortly after dosing.
  - *Oral*: In the acute oral toxicity study in male Sprague-Dawley rats that identified an LD_{50} of > 7,000 mg/kg described above for systemic toxicity and depression were seen at the high dose and resolved by day 4.
  - *Oral*: In the acute oral toxicity study in male and female mice that identified an LD_{50} of 7,000 mg/kg, animals (10sex/dose) received a single oral dose of 2.6, 4, 9, or 13.5 g/kg (route unspecified) trimethoxy(methyl)silane (purity not specified) and were observed for 10 days. At lethal doses ($\geq$ 4.0 g/kg), animals were unreactive and displayed loss of reflexes and dyspnea. Effects were similar at the lower doses, but resolved within 2 hours. Sedation and dyspnea increased in a dose dependent manner.
  - *Inhalation*: In the acute inhalation toxicity study in male and female Sprague-Dawley rats that identified an LC_{50}, > 42.1 mg/L/6h described above for systemic toxicity, animals were evaluated for autonomic and central nervous systems, motor activity and behavior pattern including tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. The only clinical signs reported were discolored urine, fecal staining, and head and muzzle soiling.
  - *Inhalation*: In the acute inhalation toxicity study in female rats that identified an LC_{50} of >144.9 mg/L, 6 animals were exposed to 26,000 ppm (144.9 mg/L) trimethoxy(methyl)silane (purity not specified) vapors for 4 hours and were observed for 14 days. Animals appeared to be anesthetized when removed from the chambers.
- Based on the weight of evidence, a score of Moderate was assigned. Anesthesia was observed in an acute inhalation study in rats, and depression, loss of reflexes, and sedation were seen in acute oral toxicity studies in rats and mice. These neurological effects suggest that GHS Category 3 classification for transient narcotic effects may be appropriate.

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

Trimethoxy(methyl)silane was assigned a score of Low for neurotoxicity (repeated dose) based on a lack of neurological effects in a 28-day oral toxicity study in rats and a 90-day inhalation toxicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate data are available and no neurological effects are seen below the guidance values of 300 mg/kg/day for in oral toxicity study (guidance value tripled due to short duration of study) or 1.0 mg/L for an inhalation toxicity study (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- ECHA 2014
  - *Oral*: In the GLP-complaint combined repeated dose toxicity study with reproductive and developmental toxicity screening test according to OECD Guideline 422 in Sprague-Dawley rats described above for systemic toxicity, neurobehavioral examinations were performed

prior to dosing and during the last week of dosing. Animals were observed for unusual body movements, abnormal behavior and/or posture, and resistance to removal, palperal closure, lacrimation, pupil size, pupil reactivity, salivation, muscle tone, extensor thrust response, reactivity to handling, level of ambulatory activity including rearing, responsiveness to sharp noise, touch, tail pinch, gait evaluation and quantity of urine and fecal pellets voided, behavior, skin or hair coat, respiration, muscle movements, eyes, urine or feces, soiling, general abnormalities and posture, rectal temperature, hindlimb/forelimb grip strength and landing foot splay. No neurobehavioral effects were seen. ToxServices identified a NOAEL of 1,000 mg/kg/day, the highest dose tested, based on the lack of effects. This is compared to tripled guidance values due to the 28-29 day length of exposure.

- *Inhalation*: In the GLP-compliant subchronic inhalation toxicity study according to OECD Guideline 413 in Crl: CD® (SD) IGS BR VAF/Plus® rats described above for systemic toxicity, clinical observations included an evaluation of autonomic and central nervous systems, motor activity, and behavior patterns. No effects were reported. Therefore ToxServices identified a NOAEC of 8.9 mg/L, the highest dose tested.

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

Trimethoxy(methyl)silane was assigned a score of Moderate for skin sensitization based on positive results in a Buehler test in guinea pigs. GreenScreen® criteria classify chemicals as a Moderate hazard for skin sensitization when available data indicate that GHS Category 1B classification is warranted (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014
  - Trimethoxy(methyl)silane (purity not specified) was sensitizing in a GLP-compliant Buehler test according to OECD Guideline 406 in male Dunkin-Hartley guinea pigs (20/test, 10/control). Animals were topically induced with a 50% solution and challenged with 25% solution for the 1st challenge and a 15% of 25% solution for the rechallenge. At challenge, positive responses were seen in 95% of animals at 24 hours and 45% of animals at 48 hours. However, positive responses were seen in 100% of negative controls at 24 hours, and 80% of negative controls at 48 hours. Positive responses were seen in 30% and 20% of test animals at 24 and 48 hours after rechallenge with the 25% solution. No positive responses were seen in negative controls. No positive responses were seen upon rechallenge with the 15% solution. Authors concluded that this substance is sensitizing by EU criteria. This study was reported with a Klimisch score of 2 for reliability, as the irritation potential was inconsistent between the preliminary and main study, and negative controls showed positive reactions in the first challenge.
  - Trimethoxy(methyl)silane was negative in a GLP-compliant Buehler test in male Dunkin-Hartley guinea pigs (20/test, 10/control) that were induced and challenged with a 50% solution. No positive responses were seen. This study was reported with a Klimisch score of 2 for reliability, as the starting concentration for induction was not the highest to cause mild-moderate skin irritation.
- Based on the weight of evidence, a score of Moderate was assigned. Two GLP-compliant Buehler tests were identified for this substance, but both were reported as reliable with restrictions. Negative results were obtained in one study, but the study did not use the highest dose to cause mild-moderate skin irritation for induction, as specified by OECD Guideline 406. A second study reported positive results in 20-30% of animals upon rechallenge with a 25% but not a 15% solution. However, in the

first challenge, positive responses were seen in both test animals and negative controls. As no positive responses were seen in the negative controls for the rechallenge, ToxServices considers the positive results in test animals during rechallenge to indicate a potential for sensitization. Positive responses in 20-30% of animals after topical induction with >20% corresponds to GHS Category 1B (> 15% responding at > 20% topical induction dose) and a score of Moderate. Confidence in this score is reduced due to inconsistency between studies and the aforementioned study deficiencies.

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

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

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): L
Trimethoxy(methyl)silane was assigned a score of Low for skin irritation/corrosivity based on negative results in two dermal irritation studies in rabbits. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when available data indicate that the chemical does not warrant GHS classification for skin irritation (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* New Zealand HSNO/GHS (GHS-New Zealand) 6.3B - Mildly irritating to the skin (Category 3)
- CCID 2014
  - Trimethoxy(methyl)silane is classified as GHS Category 2 in New Zealand based on a report in a data sheet that it is a mild irritant in rabbits. No details were provided.
- ECHA 2014
  - Trimethoxy(methyl)silane (purity not reported) was not irritating in a GLP-compliant dermal irritation study according to OECD Guideline 404 in 6 New Zealand White rabbits (sex not specified). Following a 6 hour semiocclusive administration to the shaved skin of rabbits, the mean scores at 24, 48, and 72 hours were 0.11 for erythema and 0 for edema.
  - Trimethoxy(methyl)silane (purity not reported) was not irritating in a dermal irritation study similar to OECD Guideline 404 in 6 New Zealand White rabbits (sex not specified). Following a 24-hour occlusive administration to intact skin, the mean scores at 24 and 72 hours were 1 and 0 for erythema and 0 and 0 for edema. The mean scores for abraded skin at 24 and 72 hours were 1 and 0 for erythema and 0.33 and 0.33 for edema.
- Based on the weight of evidence, a score of Low was assigned. Although it is classified as GHS Category 3 in New Zealand, this classification is based on a report in a data sheet with no supporting data. Mild irritation seen in two dermal irritation studies in rabbits, including one conducted according to GLP and OECD Guidelines, is not sufficient to classify for skin irritation, which requires mean erythema and edema score scores of $\geq$ 1.5 per GHS guidance.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): L
Trimethoxy(methyl)silane was assigned a score of Low for eye irritation/corrosivity based on negative results in a GLP-compliant ocular irritation study in rabbits. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when available data indicate that the chemical does not warrant GHS classification for eye irritation (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye (Category 2A)
- CCID 2014
  - Trimethoxy(methyl)silane is classified as a Category 2A irritant in New Zealand based on a report that it is a mild irritant in rabbits. No additional details were provided.
- ECHA 2014
  - Trimethoxy(methyl)silane (purity not reported) was not irritating in a GLP-compliant ocular irritation study according to OECD Guideline 405 in 3 New Zealand White rabbits (sex not specified). The mean scores at 24, 48, and 72 hours were 0 for the cornea, iris, conjunctiva, chemosis, and discharge. Mild to moderate conjunctival redness and discharge were seen in all animals 1 hour after instillation, but resolved by the 24 hour observation.
  - Trimethoxy(methyl)silane (purity not reported) was not irritating in an ocular irritation study in 6 New Zealand White rabbits (sex not specified) that received a single instillation (volume not specified) of a 3, 10, 30, or 100% solution. No irritation was seen at the two lowest doses. At the 3% and 100% doses, slight irritation was seen within the first 6 hours after administration but resolved within 24 hours. This study was reported in ECHA with a Klimisch score of 4 (not assignable) for reliability as information on experimental conduct was not sufficient.
  - Diffuse corneal necrosis was seen in the eyes of 4/5 rabbits (sex and strain not specified) when 0.5 mL undiluted trimethoxy(methyl)silane (purity not reported) was instilled into the eye for 24 hours. The response was graded as a score of 2/10 for corneal necrosis. The notifier notes that an excessive amount of test substance (0.5 mL rather than 0.1 mL) was used in this study.
  - Trimethoxy(methyl)silane (purity not reported) was not irritating in an ocular irritation study similar to OECD Guideline 405 in 6 albino white rabbits (sex not specified). Slight conjunctival irritation was seen in all animals and resolved by the third day. No ocular irritation scores were provided. Terminal fluorescein stain confirmed the absence of corneal damage. Authors concluded that the substance is not irritating.
- Based on the weight of evidence, a score of Low was assigned. The Category 2A classification in New Zealand, which is based on a report that this chemical is a mild irritant in rabbits, is not supported by available data. With the exception of one study that involved instillation of an excessive amount of test substance (0.5 mL rather than 0.1 mL), studies report mild irritation that resolved by 24 hours. No irritation at 24, 48, and 72 hours was seen in the GLP-compliant OECD Guideline 405 study in rabbits. Therefore a score of Low was assigned.

Ecotoxicity (Ecotox)

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

Trimethoxy(methyl)silane was assigned a score of Low for acute aquatic toxicity based on LC/EC_{50} values of greater than 200 mg/L in fish and daphnia, and greater than 120 mg/L in algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when the most conservative LC/EC_{50} values are greater than 100 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014

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- 96-hour LC_{50} (*Oncorhynchus mykiss*, rainbow trout) > 200 mg/L (nominal)
- 48-hour EC_{50} (*Daphnia magna*, water flea) > 200 mg/L (nominal)
- 72-hour EC_{50} (*Pseudokirchnerella subcapitata*, green algae) > 120 mg/L (nominal) (biomass and growth rate)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): L
Trimethoxy(methyl)silane was assigned a score of Low for chronic aquatic toxicity based on a NOEC of greater than 120 mg/L in algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- ECHA 2014
  - 72-hour NOEC (*Pseudokirchnerella subcapitata*, green algae) > 120 mg/L (nominal) (growth rate)
- Based on the weight of evidence, a score of Low was assigned. No data were identified for invertebrates or algae, but acute aquatic toxicity data do not indicate that these trophic levels are more sensitive than plants. Therefore a score of Low was assigned based on the NOEC of > 120 mg/L in algae.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *M*
Trimethoxy(methyl)silane was assigned a score of Moderate for persistence based on modeling that predicts a half-life of 30 days in soil, its major compartment. GreenScreen® criteria classify chemicals as a Moderate hazard for persistence when the half-life in soil is between 16 and 60 days (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent
- OECD 2014
  - Trimethoxy(methyl)silane's classification as persistent on the DSL is based on QSAR results predicting an ultimate degradation half-life of 15 days. The media of concern leading to categorization was air-water. A predicted atmospheric oxidation half-life of 4 days was used in the assessment.
- ECHA 2014
  - In a GLP-compliant test according to OECD Guideline 111 (Hydrolysis as a Function of pH), trimethoxy(methyl)silane had a measured hydrolysis half-life of <0.033 hours, 2.2 hours and 0.11 hours at pH 4, 7 and 9, respectively. Authors concluded that the substance is hydrolytically unstable.
- U.S. EPA 2012
  - The BIOWIN modeling Ready Biodegradable Predictor indicates that trimethoxy(methyl)silane is not expected to be readily biodegradable. Fugacity modeling predicts 72.3% will partition to soil with a half-life of 30 days, 22.1% will partition to water with a half-life of 15 days, and 5.31% will partition to air with a half-life of 4 days. See Appendix F for justification.
- Based on the weight of evidence, a score of Low was assigned. Trimethoxy(methyl)silane is not expected to be readily biodegradable, but as it undergoes rapid hydrolysis, it is not expected to

persist in the environment. Environment Canada's classification as persistent on the DSL is based on a modeled atmospheric half-life of 4 days. Current EpiSuite software (U.S. EPA 2012) predicts a half-life of 30 days in soil, which is predicted to be the chemical's dominant compartment. Therefore a score of Moderate was assigned. Confidence in this score is reduced because it is based on modeled data.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Trimethoxy(methyl)silane was assigned a score Very Low for bioaccumulation based on a modeled BCF of 0.9102. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the BCF is less than 100 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- U.S. EPA 2012
  - BCFBAF predicts a BCF of 0.9102 based on a log K_{ow} of -0.67, indicating this chemical is not likely to bioaccumulate because the BCF is less than100 based on a log K_{ow} less than 5. See Appendix F for justification.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Trimethoxy(methyl)silane was assigned a score of Low for reactivity based on reports that it is not explosive. Confidence level was reduced due to lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when the chemical is not explosive or otherwise reactive, and the chemical is not present on authoritative or screening lists (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* Not present on any screening lists
- Dow Corning 2012
  - Trimethoxy(methyl)silane is not explosive.

Flammability (F) Score (vH, H, M, or L): H
Trimethoxy(methyl)silane was assigned a score of High for flammability based on its flash point of 7.7°C and boiling point of 102°C. GreenScreen® criteria classify chemicals as a High hazard for flammability when available data indicate that GHS Category 2 classification is warranted (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists
  - *Screening:* New Zealand HSNO/GHS (GHS-New Zealand) 3.1B - Flammable Liquids: high hazard (Category 2)
- ECHA 2014
  - Trimethoxy(methyl)silane has a flash point of 7.7°C in a test according to ASTM D 3828-87 (equilibrium method closed cup).
  - Trimethoxy(methyl)silane has a boiling point of 102°C.
- Based on the weight of evidence, a score of High was assigned. Trimethoxy(methyl)silane has a flash point of 7.7°C and boiling point of 102°C. Therefore GHS Category 2 classification, which corresponds to chemicals with a flash point < 23°C and initial boiling point > 35°C, is appropriate. This is consistent with GHS classification in New Zealand, and corresponds to a score of High.

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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

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APPENDIX B: Results of Automated GreenScreen® Score Calculation for Trimethoxy(methyl)silane (CAS #1185-55-3)

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	Trimethoxy(methyl)silane	1185-55-3	*L*	*M*	L	L	*M*	L	L	M	M	L	*M*	DG	L	L	L	L	*M*	*vL*	*L*	H

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Trimethoxy(methyl)silane	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Trimethoxy(methyl)silane	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												

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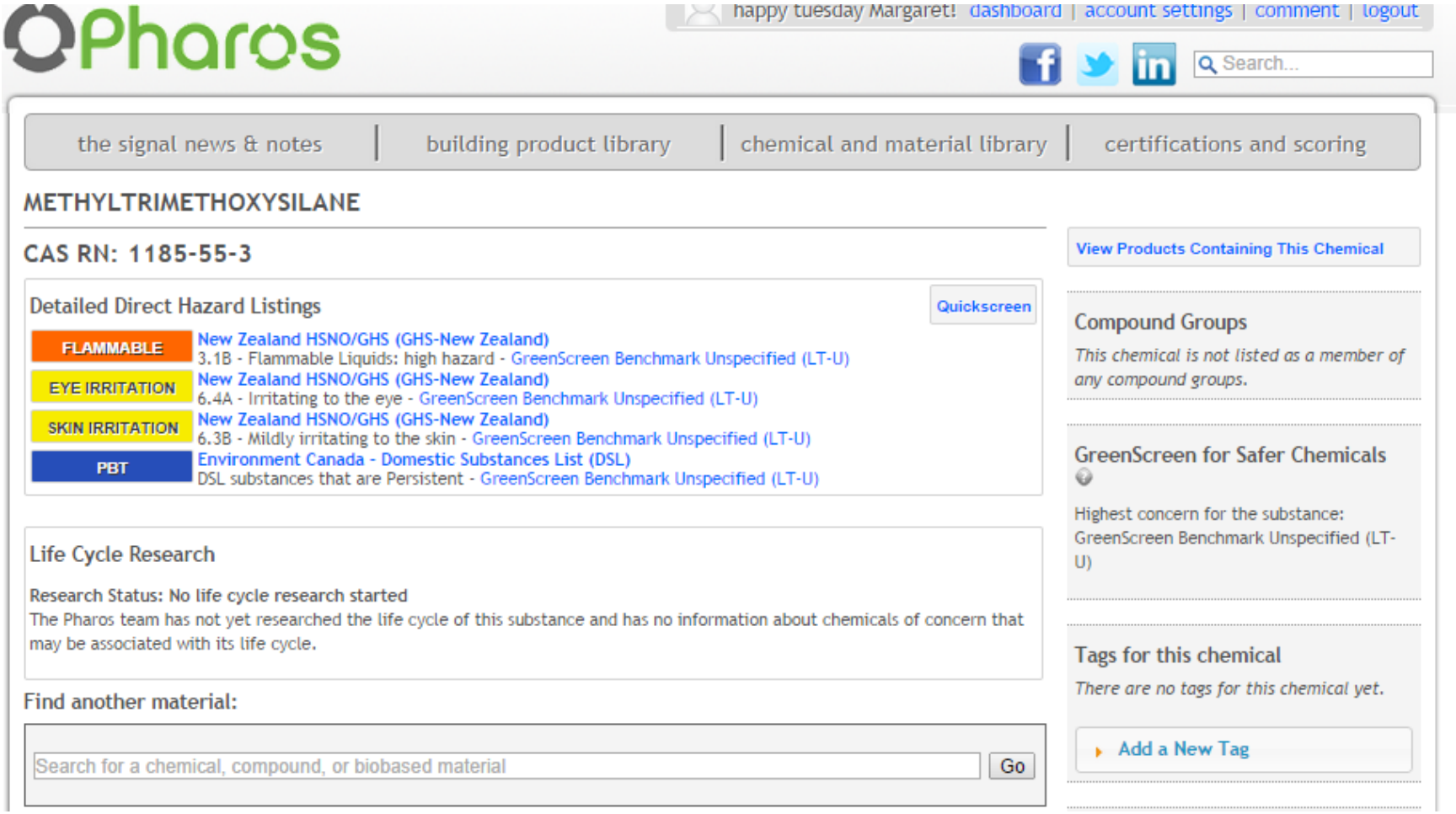
APPENDIX C: Pharos Output for Trimethoxy(methyl)silane (CAS #1185-55-3)



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APPENDIX D: OncoLogic Carcinogenicity Results for Trimethoxy(methyl)silane (CAS #1185-55-3)

OncoLogic Justification Report

SUMMARY :

Filename : 1185_55_3

Substance ID :

Si Metals or Compounds : MARGINAL

JUSTIFICATION

Si metal(s) and compounds are considered to be of MARGINAL carcinogenicity concern, due to very limited information or lack of it.

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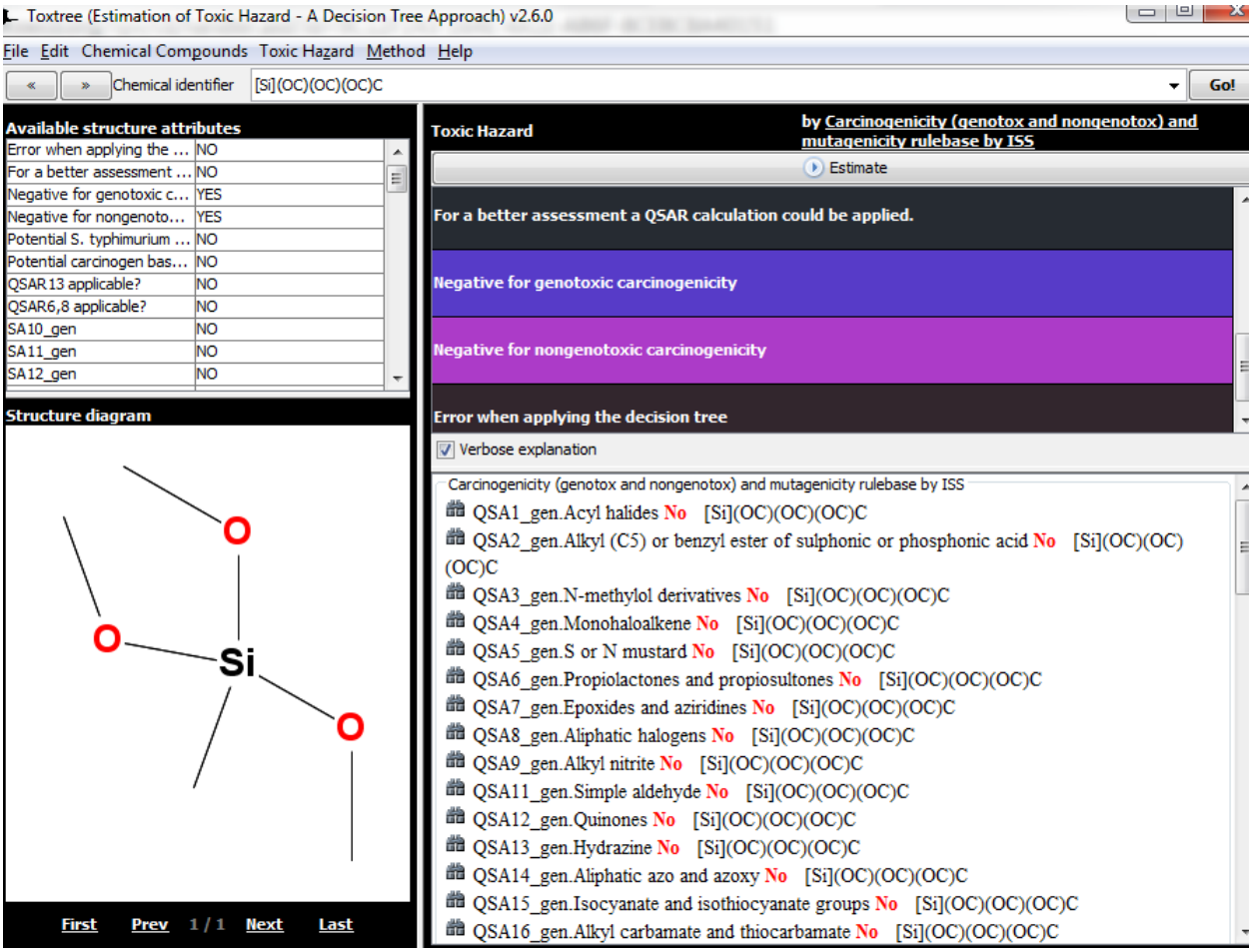
APPENDIX E: ToxTree Carcinogenicity Results for Trimethoxy(methyl)silane (CAS #1185-55-3)



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APPENDIX F: EPISuite Modeling Results for Trimethoxy(methyl)silane (CAS #1185-55-3)

CAS Number: 1185-55-3
SMILES: CO[Si](C)(OC)OC
CHEM: Methyltrimethoxysilane
MOL FOR: C4 H12 O3 Si1
MOL WT: 136.22
---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:
Log K_{ow} (octanol-water): ------
Boiling Point (deg C): 102.00
Melting Point (deg C): -77.00
Vapor Pressure (mm Hg): 22.4
Water Solubility (mg/L): ------
Henry LC (atm-m^3/mole): ------

Log Octanol-Water Partition Coef (SRC):
Log K_{ow} (K_{ow}WIN v1.68 estimate) = -0.67

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 98.41 (Adapted Stein & Brown method)
Melting Pt (deg C): -59.98 (Mean or Weighted MP)
VP (mm Hg,25 deg C): 34.4 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 4.58E+003 (Mean VP of Antoine & Grain methods)
BP (exp database): 102.5 deg C

Water Solubility Estimate from Log K_{ow} (WSK_{ow} v1.42):
Water Solubility at 25 deg C (mg/L): 1e+006
log K_{ow} used: -0.67 (estimated)
melt pt used: -77.00 deg C

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 1e+006 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Alkoxy Silanes

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 8.67E-005 atm-m^3/mole (8.79E+000 Pa-m^3/mole)
Group Method: Incomplete
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 4.015E-006 atm-m^3/mole (4.068E-001 Pa-m^3/mole)
VP: 22.4 mm Hg (source: User-Entered)
WS: 1E+006 mg/L (source: WSK_{ow}WIN)

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Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Log K_{ow} used: -0.67 (KowWin est)
Log K_{aw} used: -2.450 (HenryWin est)
Log K_{oa} (K_{oa}WIN v1.10 estimate): 1.780
Log K_{oa} (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.6827
Biowin2 (Non-Linear Model): 0.7454
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.8981 (weeks)
Biowin4 (Primary Survey Model): 3.6512 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.3085
Biowin6 (MITI Non-Linear Model): 0.2093
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.5178
Ready Biodegradability Prediction: NO

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

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 2.99E+003 Pa (22.4 mm Hg)
Log K_{oa} (K_{oa}win est): 1.780
Kp (particle/gas partition coef. (m^3/µg)):
Mackay model: 1E-009
Octanol/air (K_{oa}) model: 1.48E-011
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 3.63E-008
Mackay model: 8.04E-008
Octanol/air (K_{oa}) model: 1.18E-009

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 2.6384 E-12 cm^3/molecule-sec
Half-Life = 4.054 Days (12-hr. day; 1.5E6 OH/cm^3)
Half-Life = 48.648 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
5.83E-008 (Junge-Pankow, Mackay avg)
1.18E-009 (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 330.5 L/kg (MCI method)
Log K_{oc}: 2.519 (MCI method)
K_{oc}: 0.2619 L/kg (K_{ow} method)

Log K_{oc}: -0.582 (K_{ow} method)

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

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -1.1124 days (HL = 0.0772 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.041 (BCF = 0.9102)
Log BAF Arnot-Gobas method (upper trophic) = -0.041 (BAF = 0.9102)
log K_{ow} used: -0.67 (estimated)

Volatilization from Water:
Henry LC: 8.67E-005 atm-m^3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 9.073 hours
Half-Life from Model Lake: 196.8 hours (8.202 days)

Removal In Wastewater Treatment:
Total removal: 6.09 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.69 percent
Total to Air: 4.31 percent
(using 10000 hr. Bio P,A,S)

Removal In Wastewater Treatment:
Total removal: 75.52 percent
Total biodegradation: 73.47 percent
Total sludge adsorption: 0.61 percent
Total to Air: 1.44 percent
(using Biowin/EPA draft method)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	5.31	97.3	1000
Water	22.1	360	1000
Soil	72.3	720	1000
Sediment	0.311	3.24e+003	0

Persistence Time: 444 hr

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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/

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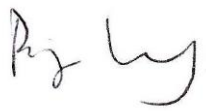

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