RTV Silicone Rubber (CAS #11099-06-2) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

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GreenScreen® Executive Summary for RTV Silicone Rubber (CAS #11099-06-2)

RTV silicone rubber is used as a binder in paints, coating, and ceramics and in precision casting.

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

- Benchmark 2f
    - High Group II* Human Toxicity (repeated dose systemic toxicity (STr*))

Data gaps (DG) exist for endocrine activity (E), single and repeated dose neurotoxicity (Ns and Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), RTV silicone rubber meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if RTV silicone rubber 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 RTV Silicone Rubber

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

GreenScreen® Assessment for RTV Silicone Rubber (CAS #11099-06-2)

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

Chemical Name: RTV Silicone Rubber

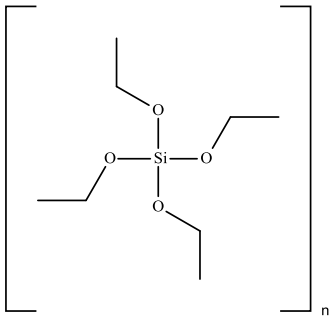
CAS Number: 11099-06-2

GreenScreen® Assessment Prepared By:
Name: Zach Guerrette, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: June 25, 2015
Assessor Type: Licensed GreenScreen® Profiler

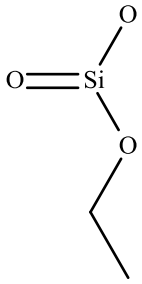
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D.,
Title: Toxicologist
Organization: ToxServices LLC
Date: June 26, 2015

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

Chemical Structure(s): The CAS number of 11099-06-2 refers to the tetraethyl orthosilicate polymer according to ChemIDplus and Pharos databases (structure shown below). In the OECD assessment of ethyl silicates group, the CAS number of 11099-06-2 refers to the oligomers and homopolymers that result from the reaction of silicic acid, ethyl ester (OECD 2008). In ECHA and EPI suite program, the CAS number of 11099-06-2 refers to silicic acid, ethyl ester (see structure below). Silicic acid, ethyl ester can hydrolyze upon contact with water to form metasilicic acid or silicic acid, which then will react to form oligomers and homopolymers (OECD 2008). One supplier of this CAS number indicates that it is a hydrolyzed and oligomerized form of ethyl silicate, which is a mixture of monomers, dimers, trimers and cyclic polysiloxanes (SiSiB Silanes 2014). ToxServices considered the structure shown in the OECD SIDS document (2008) the most likely structure of this CAS number, and assessed this CAS number as a mixture of monomers, oligomers and polymers.

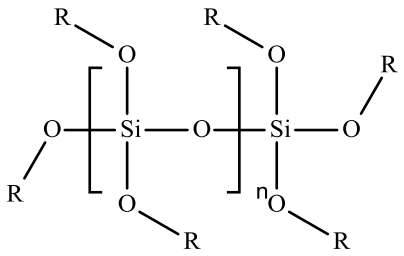


Tetraethyl orthosilicate polymer (CAS #11099-06-2)
(ChemIDplus 2015, Pharos 2015)



Silicic acid, ethyl ester (CAS #11099-06-2)
(ECHA 2015, U.S. EPA 2012)

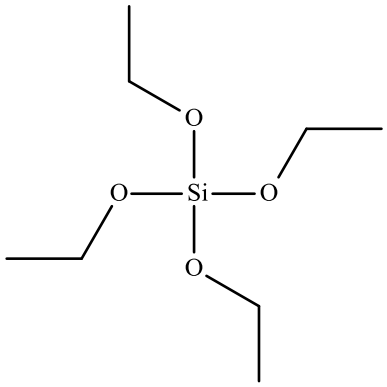
[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2
[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized 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



CAS #11099-06-2, R = ethyl or hydrogen, n = 4 is a representative example of the polymer/oligomer (OECD 2008)

Also called: Ethyl silicate**;** Polysilicic acid, ethyl ester**;** Silicic acid (H4SiO4), tetraethyl ester, homopolymer**;** Silicic acid, tetraethylester polymer**;** Tetraethyl orthosilicate polymer**;** Silicic acid, ethyl ester (ChemIDplus 2015)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
In the OECD assessment of ethyl silicates group, which included the CAS #11099-06-2, tetraethyl orthosilicate (CAS #78-10-4) was used as a surrogate where data are not available for the other members of this category. These compounds all have similar chemical structures and physicochemical (hydrolysis) properties. In addition, ECHA recommended the same substance (tetraethyl orthosilicate) as a related substance that might be used for read-across in assessing silicic acid, ethyl ester (CAS #11099-06-2). Based on this, ToxServices used tetraethyl orthosilicate (TEOS) as a surrogate for RTV silicone rubber. Where no data were available, modeling was performed using silicic acid, ethyl ester as the representative structure. In principle, monomers (i.e. TEOS/silicic acid, ethyl ester) exhibit a higher degree of toxicity than their polymers, and therefore using measured/modeled data on the surrogate TEOS is a very conservative approach.



Surrogate: Tetraethyl orthosilicate (CAS #78-10-4)

Identify Applications/Functional Uses (Wanda 2015)**:**
1 As a binder in paints, coating, ceramic and in precision casting
2. As a silicone that is room temperature vulcanized by a cross-linking agent

GreenScreen® Summary Rating for RTV Silicon Rubber[4]: RTV silicone rubber was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2014). This score is based on the following hazard score:

- Benchmark 2f
    - High Group II* Human Toxicity (repeated dose systemic toxicity (STr*))

Data gaps (DG) exist for endocrine activity (E), single and repeated dose neurotoxicity (Ns and Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), RTV silicone rubber meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if RTV silicone rubber 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 RTV Silicone Rubber

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

RTV silicone rubber (CAS#11099-06-2) is not readily biodegradable and it decomposes quickly upon contact with water (Power Chemical 2008 and OECD 2008). The expected hydrolysis products are ethanol (CAS #64-17-5), metasilicic acid (CAS #7699-41-4) or silicic acid (CAS #10193-36-9). Ethanol is an LT-1 chemical as it is an IARC Group 1 carcinogen. However, ethanol is readily biodegradable so it is unlikely to cause adverse effects. Further, the IARC classification for ethanol is applicable only for alcoholic beverages, and therefore not relevant to the current assessment. In addition, ethanol is listed on DfE's SCIL with a full green circle as a solvent. Both metasilicic acid and silicic acid are LT-U chemicals. Therefore, the transformation products do not modify the Benchmark Score for RTV silicone rubber.

[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.

Table 1: Transformation Product Summary Table						
Functional Use	**Life Cycle Stage**	**Transformation Pathway**	**Transformation Products**	**CAS #**	**Feasible and Relevant?**	**GreenScreen® List Translator Score or Benchmark Score[6,7]**
Solvent	End of Life	Hydrolysis	Ethanol	64-17-5	Yes	LT-1
NA	End of Life	Hydrolysis	Silicic acid (H_4SiO_4)	10193-36-9	Yes	LT-U
NA	End of Life	Hydrolysis	Metasilicic acid (H_2SiO_3)	7699-41-4	Yes	LT-U

Introduction

In general, RTV silicone rubber is a room temperature vulcanized silicone rubber, which requires crosslinking at elevated temperature to produce the cured rubber. It has a relatively low molecular weight and typically consists of a viscous hydroxyl-terminated silicone resin and tetraethyl orthosilicate (TEOS), the crosslinking agent. When reacted together, they form silicone rubber (Honey Silicone 2011).

The CAS number of 11099-06-2 refers to the tetraethyl orthosilicate polymer according to ChemIDplus and Pharos databases. It is considered by Environment Canada as a UVCBs-organic substance (Environment Canada 2013).

ToxServices assessed RTV silicone rubber against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.37 (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 2012a). Pharos (Pharos 2015) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for RTV silicone rubber can be found in Appendix C and a summary of the results can be found below:

- Restricted List
    - German FEA - Substances Hazardous to Waters (VwVwS) - Class 1 Low Hazard to Waters

Physiochemical Properties of RTV Silicone Rubber

RTV silicone rubber is a colorless liquid at room temperature. Its vapor can form explosive mixtures with air and it reacts with water, forming volatile ethyl alcohol (Power Chemical 2008).

Table 2: Physical and Chemical Properties of RTV Silicone Rubber (CAS #11099-06-2)		
Property	**Value**	**Reference**
Molecular formula	C_2-H_6-O.Si-Unspecified	ChemIDplus 2015
SMILES Notation	[Si](OCC)(OCC)(OCC)OCC (for the monomer)	ChemIDplus 2015
Molecular weight	740 (approximately)	Wanda 2015
Physical state	Liquid	Power Chemical 2008
Appearance	Colorless	Power Chemical 2008
Melting point	NA	

[6] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen® benchmark 1 chemicals (CPA 2012a). Pharos (Pharos 2015) 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).

Table 2: Physical and Chemical Properties of RTV Silicone Rubber (CAS #11099-06-2)		
Property	**Value**	**Reference**
Vapor pressure	< 2 hPa (20°C)	Power Chemical 2008
Water solubility	not miscible	Power Chemical 2008
Dissociation constant	NA	
Density/specific gravity	1,06 g/cm^3 (20°C)	Power Chemical 2008
Partition coefficient	NA	

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): *L*
RTV silicone rubber was assigned a score of Low for carcinogenicity based predicted data. Confidence level was reduced due to lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when negative results, no structural alerts, and no GHS classification are available (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Toxtree 2014
  - Modeling was performed using ToxTree program v2.6.6. Silicic acid, ethyl ester is predicted negative for both genotoxic and non-genotoxic carcinogenicity (see Appendix D).
- VEGA 2012
  - Silicic acid, ethyl ester is predicted to be carcinogenic with low reliability because the compound is out of the model applicability domain (See Appendix E).
- U.S. EPA 2013
  - ToxServices assessed RTV silicone rubber as a polysiloxane-type compound in OncoLogic (v 8.0), and used the ethyl groups as the terminal groups and n=4 as specified by OECD (2008) to represent its structure. The baseline of carcinogenic concern for the polysiloxane-type compound with hydrogen rather than ethyl group as the terminal groups has a low concern for carcinogenicity. The terminal ethyl groups are not expected to affect the activity of the compound. The final level of concern is marginal for the inhalation route, and low for other routes, as silylatig activity and irritation may occur through inhalation of reactive organosilicon compounds (Appendix F).

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L
RTV silicone rubber was assigned a score of Low for mutagenicity/genotoxicity based on negative *in vitro* mutagenicity tests. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data, no structural alerts, and no GHS classification are available (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- CCRIS 1999 and OECD 2008
  - Ethyl silicate (CAS#11099-06-2): Negative results for mutagenicity were obtained in an Ames test using *Salmonella typhimurium* tester strains TA 98, TA 100, TA 1535, TA 1537 and TA 102 at concentration up to 10,000 µg/plate with and without metabolic activation. No

increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.

- ECHA 2015 and OECD 2008
    - *Tetraethyl orthosilicate*: Negative results for mutagenicity were obtained in a bacterial reverse mutation assays conducted according to EU Method B.13/14. *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to tetraethyl orthosilicate in DMSO at concentration up to 5,000 µg/plate, with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation.
    - *Tetraethyl orthosilicate*: Negative results for clastogenicity were obtained in a GLP-compliant mammalian cell chromosome aberration test conducted according to OECD 473. Chinese hamster Ovary (CHO) cells were exposed to tetraethyl orthosilicate (purity not specified) at 125 to 1500 µg/ml without activation for 4 and 20h exposure, and 500 to 2080 µg/ml with activation for 4 hour exposure. No increase in the frequency of chromosome aberrations was observed with treatment in the presence or absence of metabolic activation.
    - *Tetraethyl orthosilicate*: Negative results for mutagenicity were obtained in a mammalian cell gene mutation assay conducted in a manner similar to OECD 476. Chinese hamster Ovary (CHO) cells were exposed to tetraethyl orthosilicate (purity not specified) at 0, 1.1, or 1.4 µg/mL with and without metabolic activation. No increase in the mutation frequency was observed with treatment in the presence or absence of metabolic activation.

Reproductive Toxicity (R) Score (H, M, or L): *L*
RTV silicone rubber was assigned a score of Low for reproductive toxicity based on negative results in a rat study conducted with the surrogate. Confidence level was reduced because limited relevant endpoints are examined in OECD 422 studies. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when negative data for reproductive toxicity, no structural alerts, and no GHS classification are available (CPA 2012b).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- ECHA 2015 and OECD 2008
    - *Tetraethyl orthosilicate*: In a GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD Guideline 422, Sprague-Dawley rats (10/sex/dose group) were administered tetraethyl orthosilicate (purity not specified) in corn oil by oral gavage at doses of 0, 10, 50 or 100 mg/kg/day. Male rats were exposed for 4 weeks. Reproductive phase females were dosed for two weeks prior to mating, through pregnancy, and then to postnatal day 4 (total of 45 days). The parental animals were evaluated for clinical signs of toxicity, body weight, hematology, clinical chemistry, testes, prostate and epididymis weights, gross pathology, and histopathology. Reproductive parameters (sperm measures, fertility index, mating index and gestation index) were also evaluated in parental animals. There were no treatment-related effects on any of the fertility or reproductive indices measured.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): *L*
RTV silicone rubber was assigned a score of Low for developmental toxicity based on negative results in a rat study conducted with the surrogate. Confidence level was reduced because limited relevant endpoints are examined in OECD 421 studies. GreenScreen® criteria classify chemicals as a Low hazard

for developmental toxicity when negative data for developmental toxicity, no structural alerts, and no GHS classification are available (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- ECHA 2015 and OECD 2008
  - *Tetraethyl orthosilicate*: In the previously described GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD Guideline 422, Sprague-Dawley rats (10/sex/dose group) were administered tetraethyl orthosilicate (purity not specified) in corn oil by oral gavage at doses of 0, 10, 50 or 100 mg/kg/day. Male rats were exposed for 4 weeks. Reproductive phase females were dosed for two weeks prior to mating, through pregnancy, and then to postnatal day 4 (total of 45 days). Offspring were evaluated for survival, number and sex of pups, body weight, and external abnormalities. There were no treatment-related effects on any of the fertility or reproductive indices measured. No adverse treatment-related fetal effects on fetal weight, litter size, or external, skeletal, or visceral malformations were noted at any dose level. Based on this, the study authors identified a developmental toxicity NOAEL of 100 mg/kg/day, which was the highest dose tested.

Endocrine Activity (E) Score (H, M, or L): DG

RTV silicone rubber was assigned a score of Data Gap for endocrine activity 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.
- No data were identified for this endpoint.

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

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

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

RTV silicone rubber was assigned a score of Low for acute toxicity based on its measured oral, dermal and inhalation acute toxicity values. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are greater than 2,000 mg/kg and inhalation LC_{50} values are greater than 20 mg/L (vapor) (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Power Chemical 2008
  - Ethyl polysilicate (CAS#11099-06-2): *Oral*: LD_{50} (rat) > 2,000 mg/kg
  - Ethyl polysilicate (CAS#11099-06-2): *Dermal*: LD_{50} (rat) > 2,000 mg/kg (4hr)

- Ethyl polysilicate (CAS#11099-06-2): *Inhalation*: LC_{50} (rat) > 27.1 mg/L

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)* (vH, H, M, or L): M**
RTV silicone rubber was assigned a score of Moderate for systemic toxicity (single dose) based on being self-classified to GHS category 3 (H335) supported by experimental data for the surrogate. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are classified to GHS category 3 or associated with EU hazard statement of H335 (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- C&L 2015
  - Silicic acid, ethyl ester (CAS#11099-06-2) is self-classified by 76/126 notifiers as STOT SE 3 with a hazard statement of H335: May cause respiratory irritation.
- ECHA 2015 and OECD 2008
  - Oral
    - *Tetraethyl orthosilicate*: In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 423, Wistar rats (3/sex) were administered the test material (purity not specified) in polyethylene glycol at a single dose of 2,000 mg/kg by oral gavage followed by a 14-day observation period. No mortalities or treatment-related effects on clinical signs of toxicity and body weight were seen. No abnormalities were found at macroscopic examination of the animals. An oral LD_{50} of greater than 2,000 mg/kg was identified in this study. ToxServices identified the NOAEL at 2,000 mg/kg/day for this study based on the lack of significant systemic toxicity observed.
  - Inhalation
    - *Tetraethyl orthosilicate*: In a GLP-compliant acute inhalation toxicity study conducted according to the OECD Guideline 403, Wiskf(SPF71) rats (5/sex/dose) were exposed by nose only inhalation to tetraethyl orthosilicate (purity not specified) aerosol at concentrations of 5.74, 9.98, 10.40 and 16.83 mg/L for 4 hours. Animals were then observed for 14 consecutive days. Death occurred in all dosed animals on the 3rd test day. Clinical signs of toxicity included altered motor behavior and respiration, palpebral stenosis extending to full lid closure with encrusted blood covered eyelid rims, shivering and tonic cramping. Cyanosis and decreased reflexes occurred in individual animals. Necropsy findings included red and orange lung coloration in female rats. There were no macroscopic findings in the male rats. The inhalation LC_{50} of 10.0 mg/L in male rats and 16.8 mg/L in females were identified in this study.
- Based on above data, acute exposure to the surrogate tetraethyl orthosilicate via the inhalation route led to signs of respiratory irritation such as irregular breathing patterns and labored breathing patterns. Accordingly, tetraethyl orthosilicate is classified to GHS category 3 in its RAECH registration dossier, which corresponds to a score of Moderate. No systemic toxicity was observed after oral exposures.

***Group II* Score (repeated dose)* (H, M, or L):** *H*
RTV silicone rubber was assigned a score of High for systemic toxicity (repeated dose) based on ToxServices classifying the surrogate as GHS Category 1 systemic toxicity (repeated dose). GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (repeated dose) when the

inhalation LOAEC is ≤ 0.2 mg/L/6h/day (vapor) for studies lasting at least 90 days (or 0.65 mg/L/6h/day for a 4-week study), or when they are classified to GHS category 1 (CPA 2012b).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- ECHA 2015 and OECD 2008
    - Oral
        - *Tetraethyl orthosilicate*: In the previously described GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD Guideline 422, Sprague-Dawley rats (10/sex/dose group) were administered tetraethyl orthosilicate (purity not specified) in corn oil by oral gavage at doses of 0, 10, 50 or 100 mg/kg/day. Male rats were exposed for 4 weeks. Reproductive phase females were dosed for two weeks prior to mating, through pregnancy, and then to postnatal day 4 (total of 45 days). The parental animals were evaluated for clinical signs of toxicity, body weight, hematology, clinical chemistry, testes, prostate and epididymis weights, gross pathology, and histopathology. No mortalities were observed. Females at 100 mg/kg/day showed a transient decrease in body weight gain during lactation. No change in body weight was noted in males at any dose. There were treatment-related changes in the kidney. Degenerative/necrotic nephropathy was observed in males treated with 50 mg/kg/day and above and in females at 100 mg/kg /day. This was associated with slightly lower plasma levels of sodium, potassium and glucose. Based on the observation of tubular nephropathy and associated clinical chemistry changes, the study authors identified a systemic toxicity NOAEL of 10 and 50 mg/kg/day in male and female rats, respectively. *The LOAEL of 50 mg/kg/day is within the duration adjusted GHS guidance values for category 2 of 20-200 mg/kg/day for ~45-day studies. While the NOAEL of 10 mg/kg/day is below the cutoff of 20 mg/kg/day to determine if adverse effect would occur at 20 mg/kg/day. Therefore tetraethyl orthosilicate is most likely classified to GHS category 2 with reduced confidence*.
        - *Tetraethyl orthosilicate*: In a range finding repeated dose toxicity study, Sprague-Dawley rats (3/sex/dose group) were administered tetraethyl orthosilicate (purity not specified) in corn oil by oral gavage at doses of 0, 200, 600 or 1,000 mg/kg/day for 7 days. Two male rats at the highest dose died. Significant body weight loss or decreased body weight gain was seen in both sexes at all doses. At necropsy, enlargement and abnormal coloration of the kidneys was noted in both sexes at 600 and 1,000 mg/kg/day and in one male at 200 mg/kg/day. This was correlated with high kidney weights. In males, the prostate and seminal vesicles were reduced in size. Based on this, the study authors identified a systemic toxicity LOAEL of 200 mg/kg/day, which was the lowest dose tested.
    - Inhalation (only the key study was described below)
        - *Tetraethyl orthosilicate*: In a repeated inhalation toxicity study conducted in a manner similar to OECD 412 Guideline, groups of ten ICR male mice were exposed via whole body inhalation to tetraethyl orthosilicate (purity not specified) vapor at concentrations of 50 or 100 ppm for 6 hrs/d, 5d/week for 2 or 4 weeks. The animals were evaluated for clinical signs of toxicity, body weight, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. No mortalities or treatment-related effects on body weight, clinical chemistry, or urinalysis were observed. Animals showed signs of irritation in the nasal mucosa. At the end of 4

weeks of treatment, hematological values (RBC, Hb and Ht) were lower in exposed mice. However, there was no clear dose response, and statistical significance was not always reached. Microscopic changes of the nasal mucosa were observed in all exposed mice to 100 ppm or 50 ppm for 2 or 4 weeks. Tubulo-interstitial nephritis was observed in mice exposed to 100 ppm (but not 50 ppm) for 2 or 4 weeks. Based on hematological changes, the study authors identified a LOAEC of 50 ppm; equivalent to 0.3 mg/L/6h/day[8]. *The dose of 0.3 mg/L/6h/day is below the duration-adjusted GHS guideline value for category 1 (0.65 mg/L/6h/day[9]) for 4-week studies. Therefore tetraethyl orthosilicate is classified to GHS category 1.*

- Based on the above data, the lowest oral LOAEL for the surrogate was within the cut off for GHS category 2 and the inhalation LOAEC was within the cut off for GHS category 1. Therefore ToxServices classified RTV silicone rubber to GHS category 1. The confidence level was adjusted as the surrogate may be too conservative.

Neurotoxicity (N)

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

RTV silicone rubber was assigned a score of Data Gap for neurotoxicity (single dose) 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 classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- No data were identified for this endpoint.

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

RTV silicone rubber was assigned a score of Data Gap for neurotoxicity (repeated dose) based on lack of sufficient experimental data.

- 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).
- ECHA 2015 and OECD 2008
  - *Tetraethyl orthosilicate*: In the previously described GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD Guideline 422, Sprague-Dawley rats (10/sex/dose group) were administered tetraethyl orthosilicate (purity not specified) in corn oil by oral gavage at doses of 0, 10, 50 or 100 mg/kg/day. Male rats were exposed for 4 weeks. Reproductive phase females were dosed for two weeks prior to mating, through pregnancy, and then to postnatal day 4 (total of 45 days). Neurobehavioral examination was performed on the treated rats which included FOB, sensory evaluation, grip strength and motor activity. No treatment related effects on these parameters were seen. Based on this ToxServices identified the neurotoxicity NOAEL at 100 mg/kg/day, which is the highest dose tested. *The NOAEL of 100 mg/kg/day is below the duration adjusted GHS cutoff values for a 45-day study (i.e. 20 and 200 mg/kg/day). Therefore, there was*

[8] Converting exposure period 5days/week to daily = 50ppm x 5 / 7(days) = 35.7 ppm
To convert concentrations in air (at 25ºC) from ppm to mg/L: mg/L = (ppm x molecular weight) / 24,450. The molecular weight of tetraethyl orthosilicate is 208.328 g/mol.
[9] 0.2 mg/L x 13 weeks/4 weeks = 0.65 mg/L

sufficient data to determine that tetraethyl orthosilicate is not classified to GHS category 1, but there was insufficient data to determine if it can be classified to GHS category 2.

Skin Sensitization (SnS) Group II* Score (H, M, or L): L
RTV silicone rubber was assigned a score of Low for skin sensitization based on negative findings in skin sensitization studies. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when negative results, no structural alerts, and no GHS classification are available (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Power Chemical 2008
  - Ethyl polysilicate (CAS#11099-06-2) was not a skin sensitizer when tested in a Buehler Test. No further details were provided.
- OECD 2008
  - Silicic acid, ethyl ester (PEOS) was not a skin sensitizing in guinea pigs when tested according to OECD Guideline 406 (Buehler Test).

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG
RTV silicone rubber was 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): L
RTV silicone rubber was assigned a score of Low for skin irritation/corrosivity based on negative findings in dermal irritation studies. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when negative data, no structural alerts, and no GHS classification are available (CPA 2012b)

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint
- Power Chemical 2008
  - Ethyl polysilicate (CAS#11099-06-2) was not irritating to the skin in a test conducted according to the company Guideline. No further details were provided.
- OECD 2008
  - Silicic acid, ethyl ester (PEOS) was not irritating to the skin of rabbits when tested according to FIFRA/TSCA test guideline.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): H
RTV silicone rubber was assigned a score of High for eye irritation/corrosivity based on being self-classified to GHS category 2 (H319) supported by measured data. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are classified as GHS Category 2A eye irritants or associated with EU hazard statement of H319 (CPA 2012b).

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

- Power Chemical 2008
  - Ethyl polysilicate (CAS#11099-06-2) was slightly irritating to the eye in a test conducted according to the company Guideline. No further details were provided.
- OECD 2008
  - Silicic acid, ethyl ester (PEOS) was a minimal eye irritant in rabbits when tested according to FIFRA/TSCA test guideline.
- C&L 2015
  - Silicic acid, ethyl ester (CAS#11099-06-2) is self-classified by 43/126 notifiers as Eye Irrit. 2 with a hazard statement of H319: Causes serious eye irritation.
- ECHA 2015
  - *Tetraethyl orthosilicate*: In laboratory studies using tetraethyl orthosilicate, workers were exposed to vapors of tetraethyl orthosilicate at concentrations of 85, 250, 700, 1200 and 3000 ppm. Irritation of the eyes and nose were seen at concentrations of 250 ppm and above. Concentrations of 700 ppm could be tolerated for approximately 30 minutes. Based on this, tetraethyl orthosilicate was classified as Eye Irrit. 2 in its REACH registration dossier.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
RTV silicone rubber was assigned a score of Low for acute aquatic toxicity based on its acute aquatic toxicity values being greater than 100 mg/L. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 100 mg/L (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Power Chemical 2008 and OECD 2008
  - 96-hour LC_{50} (*Brachydanio rerio,* fish) > 119 mg/L
  - 48-hour LC_{50} (*Daphnia magna*) > 193 mg/L
  - 72-hour LC_{50} (*Scenedesmus subspicatus,* green algae) > 207 mg/L

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *L*
RTV silicone rubber was assigned a score of Low for chronic aquatic toxicity based on measured data in green algae. Confidence level was reduced due to the lack of data for fish and aquatic invertebrates. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 10 mg/L (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Power Chemical 2008 and OECD 2008
  - 3-day NOEC (*Scenedesmus subspicatus,* green algae) = 115 mg/L

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *M*
RTV silicone rubber was assigned a score of Moderate for persistence based on its predicted half life data in soil. Confidence level was reduced due to lack of experimental data. GreenScreen® criteria classify chemicals as a Moderate hazard for persistence when data indicate a half-life of > 16-60 days in soil or sediment or > 16-40 days in water (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Power Chemical 2008
  - Ethyl polysilicate (CAS#11099-06-2) achieved only 47% degradation when tested in a biodegradability test (No further details available).
  - According to the material safety data sheet, ethyl polysilicate decomposes quickly upon hydrolysis and produces ethanol.
- OECD 2008
  - In a biodegradability test (modified sturm test), only 47% degradation was achieved for silicic acid, ethyl ester (No further details available).
  - The calculated hydrolysis half-life for TEOS is 4.4 hours at pH 7. The hydrolysis of silicic acid, ethyl ester (PEOS) is dependent on the solubility of the individual components. Other hydrolysis products are expected to be metasilicic acid, silicic acid and ethanol.
- U.S. EPA 2012
  - According to OECD (2008), the EPISuite™ program has not been validated to assess applicability to siloxanes/silanes/silanols. Therefore prediction results are considered not adequate. The BIOWIN modeling Ready Biodegradable Predictor indicates that silicic acid, ethyl ester is not expected to be readily biodegradable (see Appendix G). Fugacity modeling predicts 71.5% will partition to soil with a half-life of 30 days, 26.5% will partition to water with a half-life of 15 days, and 0.166% will partition to sediment with a half-life of 135 days.
- Based on weight of evidence, a score of Moderate was assigned. Data on silicic acid, ethyl ester indicate that is not readily biodegradable but it disappears rapidly in water with a maximum predicted hydrolysis half-life of 15 days. However, water is not predicted to be the predominant compartment for silicic acid, ethyl ester, and the degradation of the higher molecular weight oligomers/polymers may be slower. Measured data on the ethyl polysilicate indicate that it is degradable to some extent, but the half-life does not meet the ready biodegradability or GHS rapid degradability criteria. EPISuite™ predicts that silicic acid, ethyl ester is going to mainly partition to soil. In soil, it has a measured half-life between 16-60 days at environmental temperature (25^{o}C), which corresponds to a score of Moderate. Confidence level was reduced due to the uncertainty in the prediction results and lack of measured data.

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

RTV silicone rubber was assigned a score of Very Low for bioaccumulation based on weight of evidence and on measured log K_{ow} for the surrogate. Confidence level was reduced due to a lack of measured data. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when BCF values are ≤ 100 or the log K_{ow} values are ≤ 4 (CPA 2012b).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- ECHA 2015
  - *Tetraethyl orthosilicate*: This substance has a log K_{ow} of 3.18 at 40°C and pH of 7 when tested according to EU Method A.8 (Partition Coefficient)
  - *Tetraethyl orthosilicate*: A BCF of 3.16 was predicted for tetraethyl orthosilicate using Bcfwin v2.17. However, the authors of ECHA registration dossier stated that this value is unreliable since the EPISuite™ program has not been validated to assess applicability to siloxanes/silanes/silanols.

- OECD 2008
    - Ethyl silicates are expected to have low bioaccumulation potential based on their reactivity as both tetraethyl orthosilicate (TEOS) and silicic acid, ethyl ester (PEOS) react to form different substances through hydrolysis. The BCF for the ethyl esters cannot be predicted, but is expected to be low if hydrolysis products predominate.
- U.S. EPA 2012
    - According to OECD 2008, the EPISuite™ program has not been validated to assess applicability to siloxanes/silanes/silanols. Therefore prediction results are considered not adequate. An estimated BCF of 3.162 was calculated based on an estimated log K_{ow} of -0.72 for silicic acid, ethyl ester (Appendix G). According to GHS criteria, this BCF suggests a low potential for bioconcentration in aquatic organisms.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
RTV silicone rubber was assigned a score of Low for reactivity based on screening data for its monomer. Confidence level was reduced due to a lack of measured data. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when no GHS classification is available (CPA 2012b). The confidence in the score is adjusted as it is not based on data or on authoritative lists.

- 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 measured data were identified.
- Power Chemical 2008
    - Hydrolysis of ethyl polysilicate generates ethanol. However, the compound is not expected to undergo any "hazardous reactions".
- ECHA 2015
    - *Tetraethyl orthosilicate*: This substance is not considered an explosive or self-reactive based on lack of functional groups associated with explosive or self-reactive properties (See Appendix H).
    - *Tetraethyl orthosilicate*: This substance is not considered to have oxidizing properties as does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible material.

Flammability (F) Score (vH, H, M, or L): M
RTV silicone rubber was assigned a score of Moderate for flammability based on self-classification by the majority of notifiers to GHS category 3 (flammable liquid) and on its measured flash point. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when they are classified to GHS category 3 or 4 for flammable liquids (CPA 2012b).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- C&L 2015
    - Silicic acid, ethyl ester (CAS#11099-06-2) is self-classified by 76/126 notifiers as Flam Liquid. 3 with a hazard statement of H226: Flammable liquid and vapor.

- Power Chemical 2008
    - Ethyl polysilicate (CAS#11099-06-2) has a flash point of ≥ 63^0C. *This value is within the cut-off value for GHS category 3 (> 60^0C and ≤93^0C) for flammable liquids and therefore RTV silicone rubber is classified as a flammable liquid GHS category 4.*
- Based on the above data, RTV silicone rubber is either classified to GHS category 3 or 4 for flammable liquids, which correspond to a score of Moderate.

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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

APPENDIX B: Results of Automated GreenScreen® Score Calculation for RTV Silicone Rubber (CAS #11099-06-2)

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	**RTV Silicone Rubber**	**11099-06-2**	*L*	**L**	*L*	*L*	DG	**L**	**M**	*H*	DG	DG	**L**	DG	**L**	**H**	**L**	*L*	*M*	*vL*	*L*	**M**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
RTV Silicone Rubber	2

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

Table 6

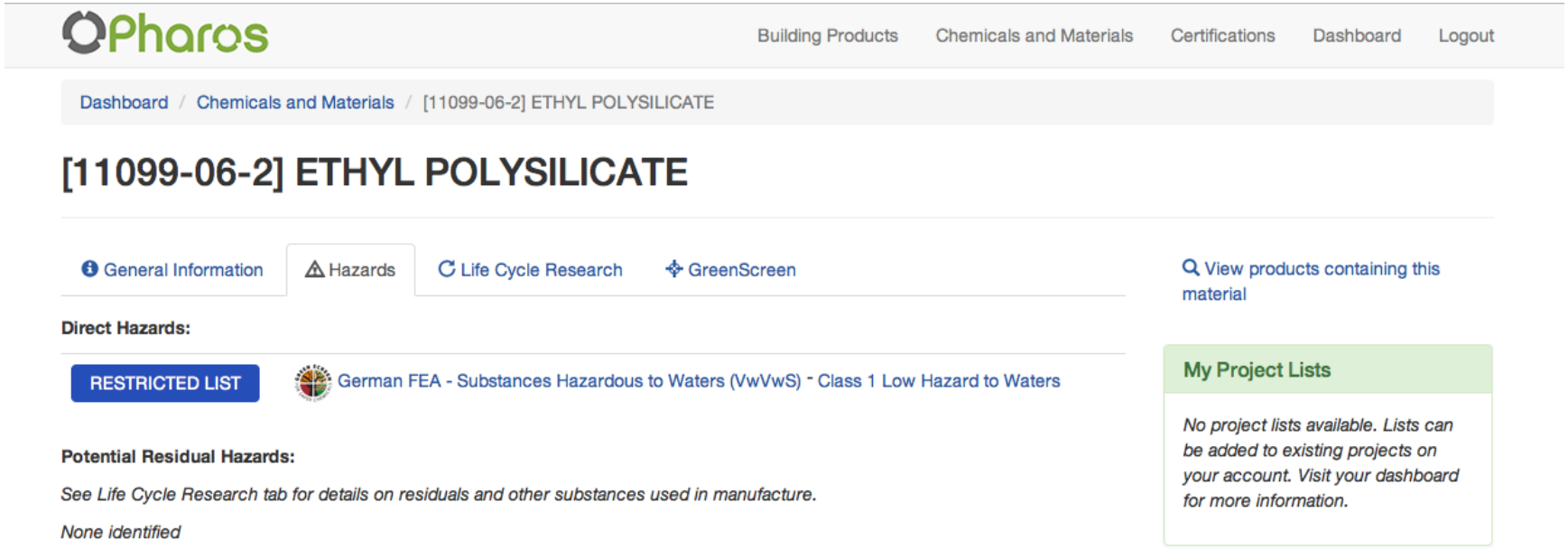
Chemical Name	Final GreenScreen® Benchmark Score
RTV Silicone Rubber	2

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

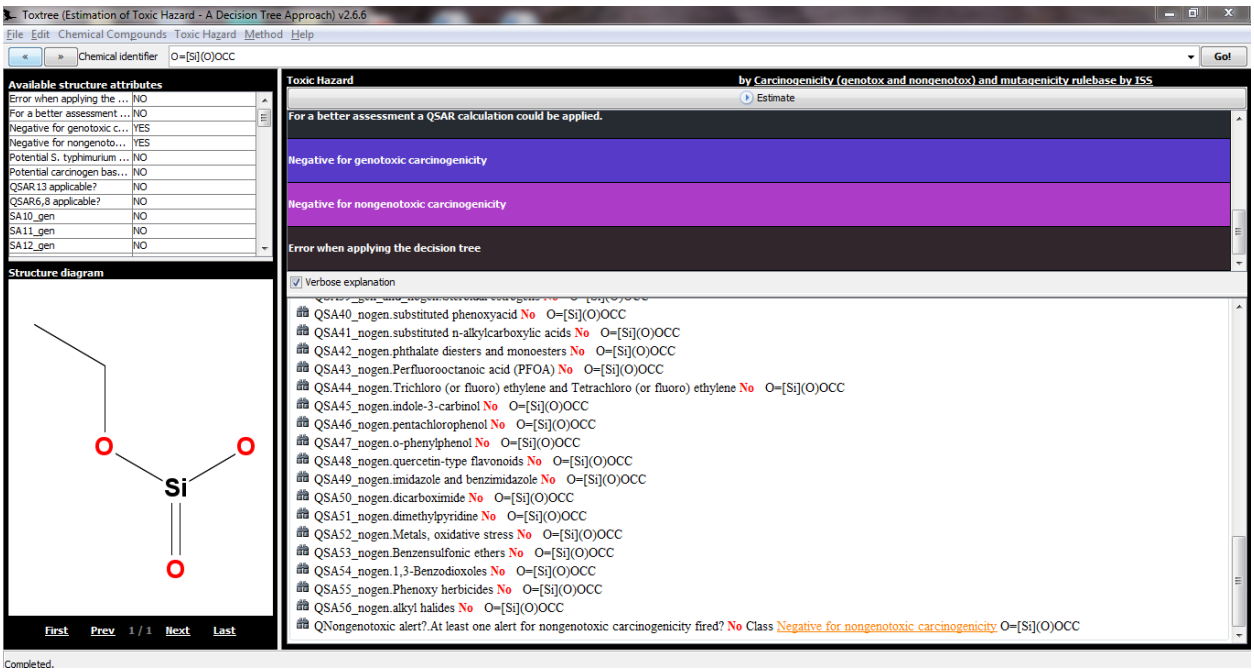
Table 5: Data Gap Assessment Table

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 RTV Silicone Rubber (CAS #11099-06-2)



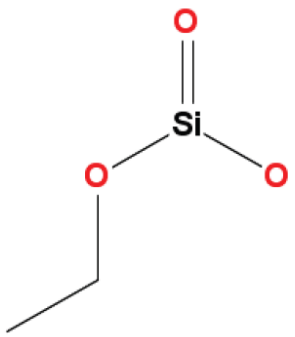
APPENDIX D: Toxtree Carcinogenicity Results for Silicic Acid, Ethyl Ester (CAS #11099-06-2)



APPENDIX E: VEGA Carcinogenicity Results for Silicic Acid, Ethyl Ester (CAS# 60177-36-8)

1. Prediction Summary

Prediction for compound 1 (Molecule 1)

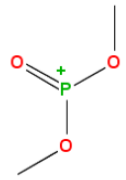


Prediction: Reliability:

Model assessment: Prediction is Carcinogen, but the result may be not reliable. Careful check of the information given in the following section should be done, paying particular attention to the following issues:
- no similar compounds with known experimental value in the training set have been found
- a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments
- predicted substance falls into a neuron that is populated by no compounds of the training set

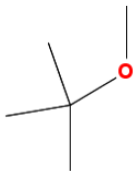
Compound: 1
Compound SMILES: O=[Si](O)OCC
Experimental value: -
Prediction: Carcinogen
Carcinogen: 0.73
NON-Carcinogen: 0.27
Structural Alerts: -
Reliability: Compound is out of model Applicability Domain
Remarks for the prediction:
none

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



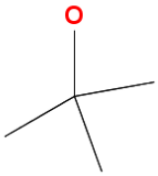
CAS: 868-85-9
Dataset id: 264 (training set)
SMILES: O=[P+](OC)OC
Similarity: 0.575

Experimental value: Carcinogen
Predicted value: Carcinogen



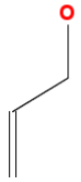
CAS: 1634-04-4
Dataset id: 444 (training set)
SMILES: O(C)C(C)(C)C
Similarity: 0.567

Experimental value: Carcinogen
Predicted value: Carcinogen



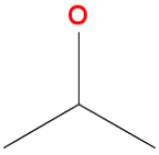
CAS: 75-65-0
Dataset id: 108 (training set)
SMILES: OC(C)(C)C
Similarity: 0.564

Experimental value: Carcinogen
Predicted value: Carcinogen



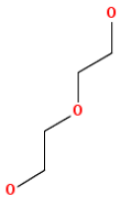
CAS: 107-18-6
Dataset id: 30 (training set)
SMILES: OCC=C
Similarity: 0.563

Experimental value: NON-Carcinogen
Predicted value: NON-Carcinogen



CAS: 67-63-0
Dataset id: 406 (training set)
SMILES: OC(C)C
Similarity: 0.559

Experimental value: NON-Carcinogen
Predicted value: NON-Carcinogen



CAS: 111-46-6
Dataset id: 240 (training set)
SMILES: OCCOCCO
Similarity: 0.551

Experimental value: Carcinogen
Predicted value: Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

✗	**Global AD Index** AD Index = 0.151 Explanation: predicted substance is outside the Applicability Domain of the model.
✗	**Similar molecules with known experimental value** Similarity index = 0.571 Explanation: no similar compounds with known experimental value in the training set have been found.
✓	**Concordance for similar molecules** Concordance index = 1 Explanation: similar molecules found in the training set have experimental values that agree with the predicted value.
✓	**Accuracy of prediction for similar molecules** Accuracy index = 1 Explanation: accuracy of prediction for similar molecules found in the training set is good.
✗	**Atom Centered Fragments similarity check** ACF matching index = 0.4 Explanation: a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments.
✓	**Model assignment reliability** Pos/Non-Pos difference = 0.458 Explanation: model class assignment is well defined.
✗	**Neural map neurons concordance** NN concordance = 0.5 Explanation: predicted substance falls into a neuron that is populated by no compounds of the training set.
✓	**Model descriptors range check** Descriptors range check = true Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set.

Symbols explanation:

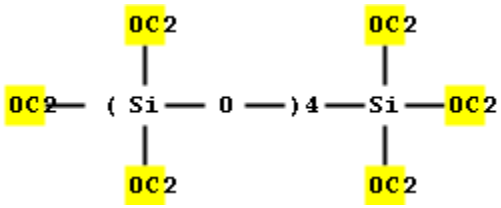
✓ The feature has a good assessment, model is reliable regarding this aspect.

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

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

APPENDIX F: OncoLogic Output for RTV Silicone Rubber (CAS #11099-06-2)

OncoLogic Justification Report



SUMMARY :

CODE NUMBER : RTV

SUBSTANCE ID :

The final level of concern for this polysiloxane-type compound, when the anticipated route of exposure is inhalation, is MARGINAL.

JUSTIFICATION:

In general, organosilicon compounds (silanes/siloxanes) are relatively unreactive and are therefore not of significant carcinogenic concern unless they contain reactive or potentially reactive moieties. However, low molecular weight organosilicon compounds which contain small alkoxy group(s) or halogen(s) linked directly to silicon are highly reactive. Although there is a scarcity of data, these alkoxysilanes and halosilanes should be of some uncertain carcinogenic concern if exposure is by inhalation because of silylating activity and irritation. For these alkoxysilanes or halosilanes, their carcinogenic potential is expected to be minimal by other routes due to the instability of the compounds upon contact with aqueous environment. An organosilicon compound which contains epoxide sidechain has been shown to be carcinogenic by the dermal route. Some organosilicon compounds which contain sidechains with terminal double bonds may also be of carcinogenic concern.

This polysiloxane-type compound where R1 is assumed to be hydrogen, R2 is assumed to be hydrogen, R3 is assumed to be hydrogen, R4 is assumed to be hydrogen, R5 is assumed to be hydrogen and R6 is assumed to be hydrogen, all linked to silicon, is not expected to be reactive. The baseline level of carcinogenicity concern is LOW.

Due to the size of the compound, the R1 ethoxy group is not expected to affect the activity of the compound.

Due to the size of the compound, the R2 ethoxy group is not expected to affect the activity of the compound.

Due to the size of the compound, the R3 ethoxy group is not expected to affect the activity of the compound.

Due to the size of the compound, the R4 ethoxy group is not expected to affect the activity of the compound.

Due to the size of the compound, the R5 ethoxy group is not expected to affect the activity of the compound.

Due to the size of the compound, the R6 ethoxy group is not expected to affect the activity of the compound.

The level of carcinogenicity concern for this compound remains LOW.

Exposure by the oral route is not expected to affect the level of concern. Therefore the level of concern for this compound remains LOW.

The final level of concern for this polysiloxane-type compound, when the anticipated route of exposure is inhalation, is MARGINAL.

APPENDIX G: EPISuite Modeling Results for Silicic Acid, Ethyl Ester (CAS #11099-06-2)

CAS Number: 11099-06-2
SMILES: O=[Si](O)OCC
CHEM: Silicic acid, ethyl ester
MOL FOR: C2 H6 O3 Si1
MOL WT: 106.15
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log K_{ow} (octanol-water): ------
Boiling Point (deg C): ------
Melting Point (deg C): ------
Vapor Pressure (mm Hg): ------
Water Solubility (mg/L): ------
Henry LC (atm-m^3/mole): ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (K_{ow}WIN v1.68 estimate) = -0.72

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 124.66 (Adapted Stein & Brown method)
Melting Pt (deg C): -62.37 (Mean or Weighted MP)
VP (mm Hg,25 deg C): 5.44 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 726 (Mean VP of Antoine & Grain methods)

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: -0.72 (estimated)
no-melting pt equation used

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

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: Incomplete
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: 7.598E-007 atm-m^3/mole (7.699E-002 Pa-m^3/mole)
VP: 5.44 mm Hg (source: MPBPVP)
WS: 1E+006 mg/L (source: WSK_{ow}WIN)

Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Can Not Estimate (can not calculate HenryLC)

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.6970
Biowin2 (Non-Linear Model): 0.8178
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.9646 (weeks)
Biowin4 (Primary Survey Model): 3.6946 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.4462
Biowin6 (MITI Non-Linear Model): 0.4775
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.7825
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): 664 Pa (4.98 mm Hg)
Log K_{oa} (): not available
Kp (particle/gas partition coef. (m^3/µg)):
Mackay model: 4.52E-009
Octanol/air (K_{oa}) model: not available
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 1.63E-007
Mackay model: 3.61E-007
Octanol/air (K_{oa}) model: not available

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 9.6234 E-12 cm^3/molecule-sec
Half-Life = 1.111 Days (12-hr day; 1.5E6 OH/cm^3)
Half-Life = 13.337 Hrs.
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
2.62E-007 (Junge-Pankow, Mackay avg)
not available (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 110.6 L/kg (MCI method)
Log K_{oc}: 2.044 (MCI method)
K_{oc}: 0.237 L/kg (K_{ow} method)
Log K_{oc}: -0.625 (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) = -1.7606 days (HL = 0.01735 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.045 (BCF = 0.9014)
Log BAF Arnot-Gobas method (upper trophic) = -0.045 (BAF = 0.9014)
log K_{ow} used: -0.72 (estimated)

Volatilization from Water:
Henry LC: 7.6E-007 atm-m^3/mole (calculated from VP/WS)
Half-Life from Model River: 795 hours (33.12 days)
Half-Life from Model Lake: 8759 hours (364.9 days)

Removal in Wastewater Treatment:
Total removal: 1.89 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.75 percent
Total to Air: 0.04 percent
(using 10000 hr. Bio P,A,S)

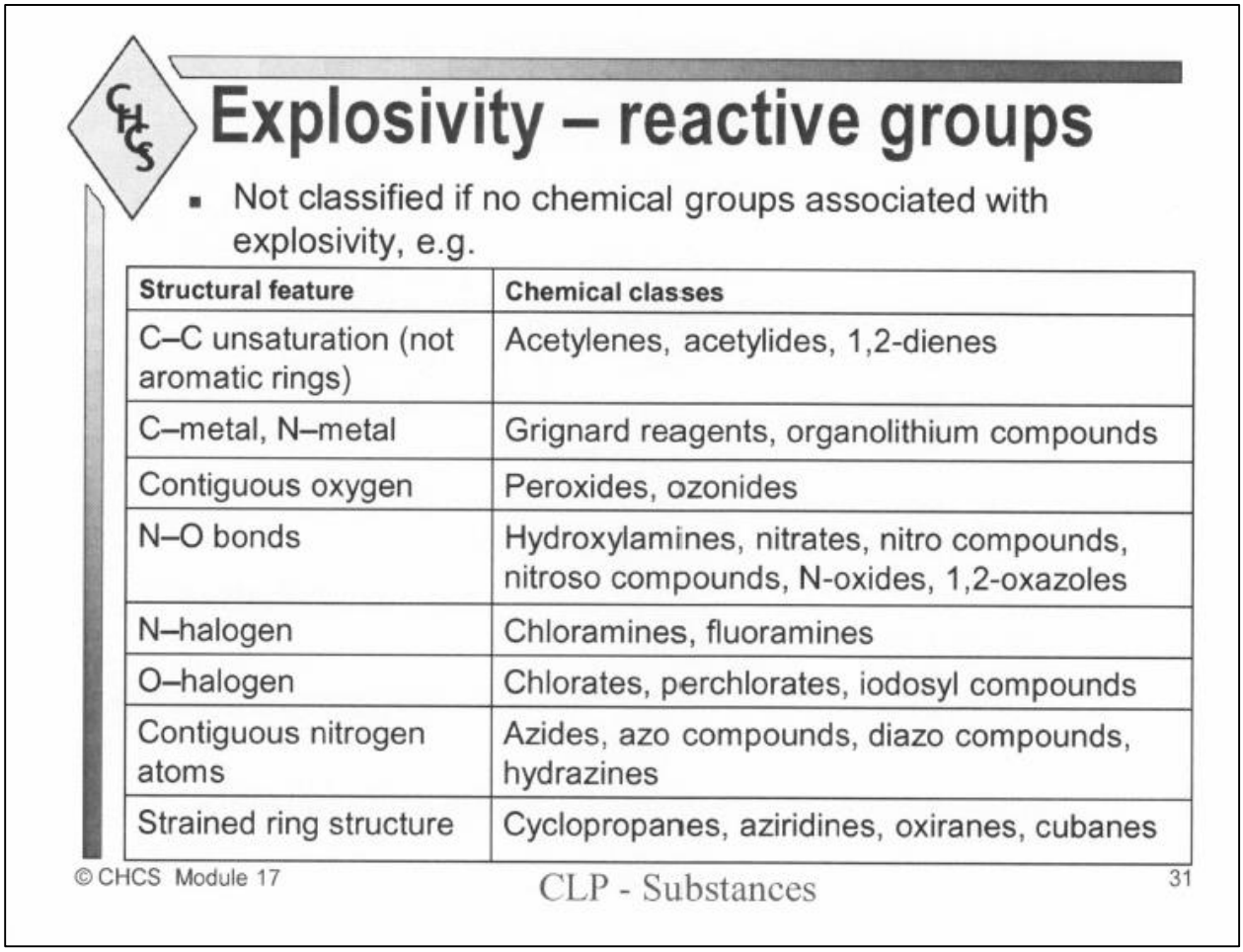
Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr.)	Emissions (kg/hr.)
Air	1.79	26.7	1000
Water	26.5	360	1000
Soil	71.5	720	1000
Sediment	0.166	3.24e+003	0

Persistence Time: 474 hr.

APPENDIX H: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

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

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

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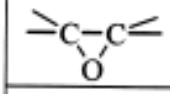
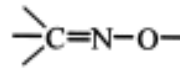
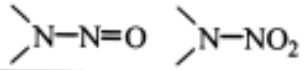
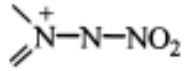
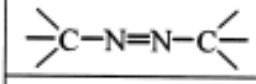
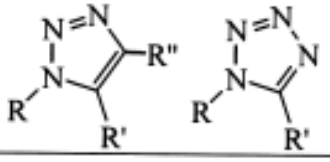
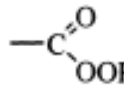
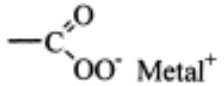
Explosivity – Full List

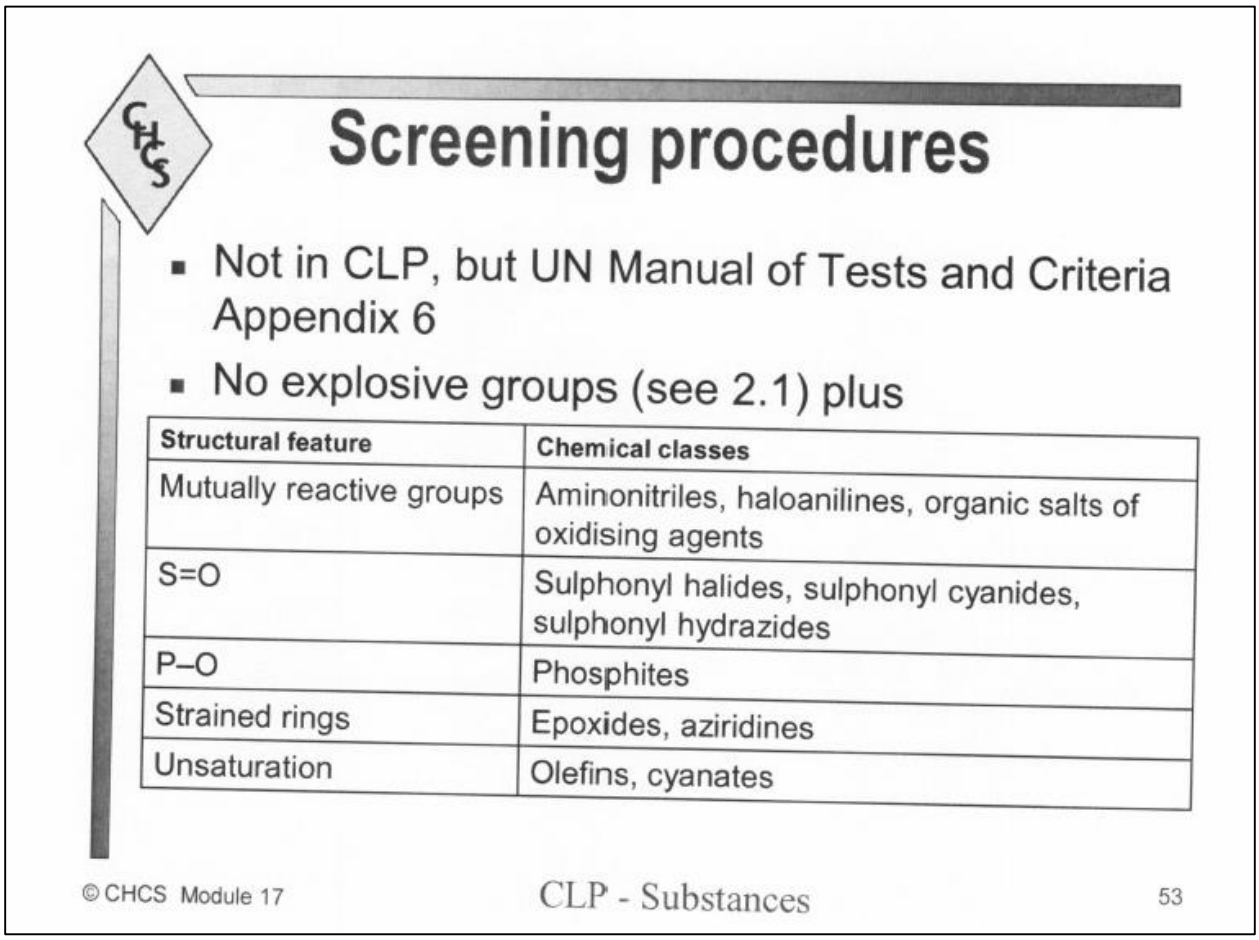
Table R.7.1-28 Chemical groups associated with explosive properties

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

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

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

Self-Reactive Substances

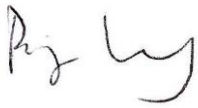


Licensed GreenScreen® Profilers

RTV Silicone Rubber GreenScreen® Evaluation Prepared by:

Zach Guerrette, Ph.D.
Toxicologist
ToxServices LLC

RTV Silicone Rubber GreenScreen® Evaluation QC'd by:



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