Amorphous Silica (Modified) (CAS #68909-20-6) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

Washington States Department of Ecology

Prepared by:

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October 17, 2014

TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Amorphous Silica (Modified) (CAS #68909-20-6)

Amorphous silica (modified) is a chemical that functions as a component of toner, cosmetics, silicone rubber, reinforcing agents, paints and lacquers, and free flow agents.

Inhalation: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of 1 ("Avoid-Chemical of High Concern") as it has Very High persistence (P) and Very High Group II Human hazard (acute toxicity (AT)) and High Group II* Human Health hazard (repeated dose systemic toxicity (ST*)). This corresponds to GreenScreen® benchmark classification 1C ("vPT = very High P + [very High T (Ecotoxicity or Group II Human) or High T (Group I or II* Human)]") in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), amorphous silica (modified) meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E) and respiratory sensitization (SnR*), it would still be categorized as a Benchmark 1 Chemical. This assessment assumes that there is no crystalline silica present in this material since the crystalline forms of silica are known human carcinogens via the inhalation route of exposure.

Oral: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has Very High persistence (P), High single dose systemic toxicity (ST), and High single dose neurotoxicity (N). This corresponds to GreenScreen® benchmark classification 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)") in CPA 2011. Data gaps (DG) exist for endocrine activity (E), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), amorphous silica (modified) meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

Dermal: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of U ("Unspecified Due to Insufficient Data") as it does not meet the minimum data requirements for a Benchmark Score of 2, based on its High acute toxicity (AT) and Very High persistence (P). This corresponds to GreenScreen® benchmark classification 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)") in CPA 2011. Data gaps (DG) exist for endocrine activity (E), repeated dose systemic toxicity (ST*), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), amorphous silica (modified) does not meet requirements for a GreenScreen® Benchmark Score of 2 due to the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E), repeated dose systemic toxicity (ST*), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
In order to address the route specified hazards, all exposure routes (oral, dermal, and inhalation) were evaluated separately and GreenScreen® Benchmark Scores were generated for each route of exposure.

GreenScreen® Hazard Ratings for Amorphous Silica (Modified)

Route of Exposure	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*										
Inhalation	L	L	L	L	DG	vH	L	H	L	L	L	DG	L	L	L	M	*vH*	*vL*	*L*	L
Oral						L	H	L	H	DG										
Dermal						H	L	DG	L	DG										

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

GreenScreen® Assessment for Amorphous Silica (Modified) (CAS #68909-20-6)

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

Chemical Name: Amorphous Silica (Modified)

CAS Number: 68909-20-6

GreenScreen® Assessment Prepared By:
Name: Zach Guerrette, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: October 3, 2014
Assessor Type: Licensed GreenScreen® Profiler

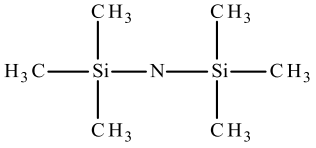
Quality Control Performed By:
Name: Dr. Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: October 17, 2014

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

Chemical Structure(s):
No chemical structure was identified for amorphous silica (modified).

Also called:
EINECS 272-697-1; Hexamethyldisilazane, silica reaction product; Hydrolysis products of 1,1,1-trimethyl-N-(trimethylsilyl)silanamine with silica; Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica; Hexamethyl disilizane, reaction product with silica, minimum number average molecular weight (in amu), 645,000 (ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
Limited data were identified for amorphous silica (modified). It is described as the reaction product betweeen hexamethyldisilazane (CAS #999-97-3) and silica (CAS #7631-86-9) (ChemIDplus 2014). ToxServices identified these two chemicals as surrogates for amorphous silica (modified) and used data for these two chemicals (illustrated below) to address the data gaps for amorphous silica (modified).



Hexamethyldisilazane
(CAS #999-97-3)

[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

Silica, amorphous
(CAS #7631-86-9)

Identify Applications/Functional Uses (Evonik 2010)**:**
1. Toner
2. Cosmetics
3. Silicone rubber
4. Reinforcing agents
5. Paints and lacquers
6. Free flow agents

GreenScreen® Summary Rating for Amorphous Silica (Modified)[4]:
Inhalation: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of 1 ("Avoid-Chemical of High Concern") as it has Very High persistence (P) and Very High Group II Human hazard (acute toxicity (AT)) and High Group II* Human Health hazard (repeated dose systemic toxicity (ST*)). This corresponds to GreenScreen® benchmark classification 1c ("vPT = very High P + [very High T (Ecotoxicity or Group II Human) or High T (Group I or II* Human)]") in CPA 2011, 2012a. Data gaps (DG) exist for endocrine activity (E) 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), amorphous silica (modified) meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E) and respiratory sensitization (SnR*), it would still be categorized as a Benchmark 1 Chemical. This assessment assumes that there is no crystalline silica present in this material since the crystalline forms of silica are known human carcinogens via the inhalation route of exposure.

Oral: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has Very High persistence (P), High single dose systemic toxicity (ST), and High single dose neurotoxicity (N). This corresponds to GreenScreen® benchmark classification 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)") in CPA 2011, 2012a. Data gaps (DG) exist for endocrine activity (E), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), amorphous silica (modified) meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

Dermal: Amorphous silica (modified) was assigned a GreenScreen® Benchmark Score of U ("Unspecified Due to Insufficient Data") as it does not meet the minimum data requirements for a Benchmark Score of 2, based on its High acute toxicity (AT) and Very High persistence (P). This corresponds to GreenScreen® benchmark classification 2c ("High P + Moderate T (Ecotoxicity or Group I, II, or II* Human)") in CPA 2011, 2012a. Data gaps (DG) exist for endocrine activity (E), repeated

[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.

dose systemic toxicity (ST*), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), amorphous silica (modified) does not meet requirements for a GreenScreen® Benchmark Score of 2 due to the hazard data gaps. In a worst-case scenario, if amorphous silica (modified) were assigned a High score for the data gaps endocrine activity (E), repeated dose systemic toxicity (ST*), repeated dose neurotoxicity (Nr*), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Amorphous Silica (Modified)

Route of Exposure	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*										
Inhalation	L	L	L	L	DG	vH	L	H	L	L	L	DG	L	L	L	M	*vH*	*vL*	*L*	L
Oral						L	H	L	H	DG										
Dermal						H	L	DG	L	DG										

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

Transformation Products and Ratings:

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

No information was identified for transformation products of amorphous silica (modified). Therefore, the Benchmark Score is not modified by the transformation products.

Introduction

Amorphous silica (modified) is used in toner, cosmetics, silicone rubber, reinforcing agents, paints and lacquers, and free flow agents (Evonik 2010). It is a reaction product of hexamethyldisilazane and silica (ChemIDplus 2014).

ToxServices assessed amorphous silica (modified) 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

[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.

human health and environmental endpoint. The output for amorphous silica (modified) can be found in Appendix C and a summary of the results can be found below:

- Amorphous silica (modified) is not listed with any high or medium hazards in Pharos.
- Amorphous silica (modified) is not listed on the U.S. DOT (2008a,b) lists.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3 (see Appendix D)
    - High hazard
        - Eye Irritation
            - GHS New Zealand Category 8.3A (equivalent to GHS Category 1 skin irritant) – corrosive to ocular tissue
        - Skin Irritation
            - GHS New Zealand Category 8.2C (equivalent to GHS Category 1 eye irritant) – corrosive to dermal tissue
        - Flammability
            - GHS New Zealand Category 3.1B (equivalent to GHS Category 2 flammable liquid) – flammable liquids: high hazard
    - Medium hazard
        - Acute Toxicity
            - GHS New Zealand Category 6.1D (oral, inhalation, dermal) (equivalent to GHS Category 4 oral, inhalation, and dermal toxicant) – acutely toxic
- Surrogate: Silica, amorphous, CAS #7631-86-9 (see Appendix E)
    - High hazard
        - Carcinogenicity
            - US CDC NIOSH occupational carcinogen

PhysicoChemical Properties of Amorphous Silica (Modified)

Amorphous silica (modified) is a white powder under standard temperature and pressure. It is insoluble in water and has a density of 2 g/cm^3 at 20°C. No other information was identified.

Table 1: Physical and Chemical Properties of Amorphous Silica (Modified) (CAS #68909-20-6)

Property	Value	Reference
Molecular formula	C6-H19-N-Si2.O2-Si	ChemIDplus 2014
SMILES Notation	Not identified	
Molecular weight	Not identified	
Physical state	Solid	Evonik 2010
Appearance	White powder	Evonik 2010
Melting point	Not identified	
Vapor pressure	Not identified	
Water solubility	Insoluble	Evonik 2010
Dissociation constant	Not identified	
Density/specific gravity	2 g/cm^3 at 20°C	Evonik 2010
Partition coefficient	Not identified	

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for carcinogenicity based on negative results for the surrogate silica, amorphous. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when negative data, no structural alerts, and no GHS classification are available (CPA 2012a). This hazard score assumes there is no crystalline silica present in amorphous, silica (modified).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - No data were identified for this endpoint.
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - Authoritative Lists
    - NIOSH-C – Occupational carcinogen when in the crystalline or fused form.
  - Screening Lists
    - IARC - Group 3: Agent is not classifiable as to its carcinogenicity to humans
  - EC 2000
    - Male and female Fischer 344 rats were given 1.25, 2.5, or 5% fumed silica (equivalent to 143.46, 179.55, or 581.18 g for male rats and 107.25, 205.02, or 435.33 g for female rats, respectively) in their feed daily for 103 weeks. Tumor incidence in testes, mammary glands, prepuce, and clitoris were higher in the controls than they were in the treated groups. Fumed silica was not carcinogenic under these test conditions.
    - Male and female B6C3F1 mice were given 1.25, 2.5, or 5% fumed silica (equivalent to 38.45, 79.78, or 160 g for male mice and 37.02, 72.46, or 157.59 g for female mice, respectively) in their feed daily for 93 weeks. While there were tumors found in the hematopoietic organs, the incidence of these lesions was not significant compared to control animals. While there were lung adenomas found, they were found to be neither sex- nor dose-related. Non-neoplastic lesions were seen in the subcutis, lungs, kidneys, and liver in the treated groups; however, these were found to be of no toxicological significance.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for mutagenicity/genotoxicity based on the negative results for mutagenicity and clastogenicity for it and the surrogate hexamethyldisilazane and silica amorphous. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative results for mutagenicity and clastogenicity, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - Evonik 2010

        - Amorphous silica (modified) was not mutagenic in an Ames test performed with *Salmonella typhimurium* and *Escherichia coli*. No further details were provided.
    - Cabot 2007
        - Amorphous silica (modified) was not mutagenic in an Ames test and was negative in a chromosome aberration test performed with Chinese hamster ovary (CHO) cells. No further details were provided.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - ECHA 2014
        - *In vitro*: egative results for clastogenicity were obtained in a GLP-compliant chromosome aberration test conducted according to OECD 473. Human lymphocytes were exposed to hexamethyldisilazane (purity not specified) at 0-1,614 µg/mL with and without metabolic activation. No increase in the frequency of chromosome aberrations was observed with treatment in the presence or absence of metabolic activation.
        - *In vitro:* Negative results for mutagenicity were obtained in a GLP-compliant Ames test conducted in a manner similar to OECD 471 (incomplete testing with positive controls with metabolic activation). *S. typhimurium* tester strains TA 98, TA 100, TA 102, TA 1535, and TA 1537 were exposed to hexamethyldisilazane (98.8% purity) at 8-5,000 µg/plate, with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation.
        - *In vitro:* Negative results for mutagenicity were obtained in a GLP-compliant mammalian cell gene mutation assay conducted according to OECD 476. Mouse lymphoma L5178Y cells were exposed to hexamethyldisilazane (purity not specified) at 0.8-10 µl/mL without metabolic activation and 0.5-5.1 µl/mL with metabolic activation.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - CCRIS 2008
        - *In vivo*: A mutagenicity study was performed using rat alveolar cells from male F344 rats. The silica was administered via inhalation at a dose of 50 mg/m^3 for 6 hours per day, 5 days per week for 13 weeks and determined to be negative.
    - EC 2000
        - *In vitro:* Not mutagenic in a number of Ames mutation studies. The tests were conducted with *Salmonella typhimurium* tester strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538, *Escherichia coli* strain WP2, and *Saccharomyces cerevisiae* strain D-3. Strains were tested at concentrations ranging from 33-10,000 µg/plate in the presence and absence of metabolic activation.
        - *In vitro*: A HGPRT assay conducted using Chinese hamster ovary (CHO) cells tested at concentrations ranging from 100-500 µg/mL in the presence of metabolic activation and 10-250 µg/mL in the absence of metabolic activation was found to be negative.
        - *In vitro*: An unscheduled DNA synthesis (UDS) assay conducted using primary rat hepatocytes tested at concentrations ranging from 0.3-1,000 µg/mL in the absence of metabolic activation was found to be negative.
        - *In vitro:* A cytogenetic assay conducted using human embryonic lung cells (Wi-38) exposed to FDA-Compound 71-48 (silica aerogel) at 1-1,000 µg/mL produced negative results for chromosome aberrations.

- *In vitro*: A cytogenetic assay was performed with CHO cells exposed to Cab-O-Sil EH-5 (fumed silica) at 19-300 µl/mL (equivalent to 41.8-660 mg/mL based on a density of 2.2 g/cm^3) without metabolic activation and 250-1,000 µl/mL (equivalent to 550-2,200 mg/mL based on a density of 2.2 g/cm^3) with metabolic activation. Negative results were observed for chromosomal aberrations in the presence and absence of metabolic activation.
- *In vivo:* Cytogenetic assays conducted using Sprague-Dawley rats given oral doses of 1.4, 14, or 140 mg/kg via gavage were found to be negative for both chromosomal aberrations and dominant-lethal effects.

Reproductive Toxicity (R) Score (H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for reproductive toxicity based on the lack of effects on reproduction in studies of the surrogates hexamethyldisilazane and silica, amorphous. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014
    - A GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD 422 was performed with Sprague-Dawley rats (10/sex/dose group, additional 10 females for toxicity group) administered whole body inhalation exposures of hexamethyldisilazane (purity not specified) vapor at 0.16, 0.66, or 2.66 mg/L for 6 hours/day for 7 days/week. Males were exposed for 14 days prior to mating and then post mating for up to 28 days in total. Females were exposed for 14 days prior to mating, during the mating and gestational periods, and to postnatal days 1-3 for up to 42 days in total. The animals were evaluated for the mating and fertility indices and testes weights. No treatment-related effects were observed on the reproductive indices, the number of corpora lutea and number of uterine implantation sites, duration of gestation, mean litter size, or mean live litter size. The study authors identified a reproductive NOAEC of 2.66 mg/L based on the lack of treatment-related reproductive effects at up to the highest concentration tested.
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - EC 2000
    - A one generation reproductive toxicity study was conducted using male and female Wistar rats. Males received 497 mg/kg and females received 509 mg/kg Aerosil (fumed silica) daily via their feed for 4.5 months prior to mating. There were no clinical symptoms, behavioral or developmental changes, or changes in any other examined parameters in pups. The NOAEL in both the F_0 and F_1 generations was at least 497 mg/kg/day.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for developmental toxicity based on the lack of developmental effects observed in studies of the surrogates hexamethyldisilazane and silica,

amorphous. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014
    - A GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD 422 was performed with Sprague-Dawley rats (10/sex/dose group, additional 10 females for toxicity group) administered whole body inhalation exposures of hexamethyldisilazane (purity not specified) vapor at 0.16, 0.66, or 2.66 mg/L for 6 hours/day for 7 days/week. Females were exposed for 14 days prior to mating, during the mating and gestational periods, and to postnatal days 1-3 for up to 42 days in total. The maternal evaluations consisted of body weight gains and the ovarian and uterine content. Pup evaluations consisted of pup viability, average pup weight, litter weights, sex ratio, and the incidences of external, visceral, and skeletal abnormalities. Decreases in absolute body weight and total body weight gain were observed for high concentration females and a decrease in absolute body weight was observed in the mid concentration females. No treatment-related effects were observed on the developmental parameters and the study authors identified a developmental NOAEC of 2.66 mg/L based on the lack of treatment-related developmental effects at up to the highest concentration tested.
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - EC 2000
    - Female Wistar rats were given oral doses of FDA-Compound 71-48 (Syloid, silica aerogel) at 0, 13.5, 62.7, 292, or 1,350 mg/kg/day via gavage from days 6-15 of gestation. There were no clearly discernible effects on nidation or maternal or fetal survival. The number of abnormalities seen in soft and skeletal tissues in the test groups did not differ from the control groups. The maternal NOAEL value was at least 1,340 mg/kg/day and the teratogenic value was 1,350 mg/kg/day.
    - Female CD-1 mice were given oral doses of FDA-Compound 71-48 (Syloid, silica aerogel) at 0, 13.4, 62.3, 289, or 1,340 mg/kg/day via gavage from days 6-15 of gestation. There were no clearly discernible effects on nidation or maternal or fetal survival. The number of abnormalities seen in soft and skeletal tissues in the test groups did not differ from the control groups. The maternal NOAEL value was at least 1,340 mg/kg/day and the teratogenic value was 1,350 mg/kg/day.
    - Dutch rabbits were given oral doses of FDA-Compound 71-48 (Syloid, silica aerogel) at 0, 16, 74.3, 345, or 1,600 mg/kg/day via gavage from days 6-18 of gestation. There were no clearly discernible effects on nidation or maternal or fetal survival. The number of abnormalities seen in soft and skeletal tissues in the test groups did not differ from the control groups. The maternal and teratogenic NOAEL values were at least 1,600 mg/kg/day.
    - Outbred Syrian hamsters were given oral doses of FDA-Compound 71-48 (Syloid, silica aerogel) at 0, 16, 74.3, 345, or 1,600 mg/kg/day via gavage from days 6-10 of gestation. There were no clearly discernible effects on nidation or maternal or fetal

survival. The number of abnormalities seen in soft and skeletal tissues in the test groups did not differ from the control groups. The maternal and teratogenic NOAEL values were at least 1,600 mg/kg/day.

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

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - No data were identified for this endpoint.
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - 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): vH (inhalation), **L** (oral), **H** (dermal)
Amorphous silica (modified) was assigned a score of Very High for acute toxicity via the inhalation route based on the inhalation LC_{50} value of 10 mg/L for the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a Very High hazard for acute toxicity when inhalation LC_{50} values are no greater than 10 mg/L (CPA 2012a). Amorphous silica (modified) was assigned a score of Low for acute toxicity based on the oral LD_{50} of greater than 2,000 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral LD_{50} values are greater than 2,000 mg/kg (CPA 2012a). Amorphous silica (modified) was assigned a score of High for acute toxicity via the dermal route based on the dermal LD_{50} values of 547-589 mg/kg for the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a High hazard for acute toxicity when dermal LD_{50} values are greater than 200 to 1,000 mg/kg (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - Evonik 2010
    - *Oral*: LD_{50} (rat) = greater than 2,000 mg/kg (OECD 401)
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - Screening lists:

        - GHS New Zealand Category 6.1D (oral, inhalation, dermal) (equivalent to GHS Category 4 oral, inhalation, and dermal toxicant) – acutely toxic
            - Based on R-phrase from company data.
    - ECHA 2014
        - *Oral*: LD_{50} (Wistar rat) = 851 mg/kg (similar to OECD 401)
        - *Inhalation:* 6-hour whole body vapor LC_{50} (Sprague-Dawley rat) = 1,516 ppm (equivalent to 10 mg/L) (GLP-compliant, OECD 403)
        - *Dermal:* LD_{50} (New Zealand White rabbit) = 589 mg/kg (males) and 547 mg/kg (females) (non-GLP-compliant, OECD 402)
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - EC 2000
        - *Oral*: LD_{50} values in rats range from greater than 5,000 mg/kg to greater than 20,000 mg/kg (as chemically prepared silicon dioxide).
        - *Dermal*: LD_{50} values in rabbits range from greater than 2,000 mg/kg to greater than 5,000 mg/kg (as chemically prepared silicon dioxide).
        - *Inhalation*: A 1-hour LC_{50} value of greater than 2.2 mg/L was determined in the rat (as chemically prepared silicon dioxide).

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)* (vH, H, M, or L): L** (inhalation), **H** (oral), **L** (dermal)
Amorphous silica (modified) was assigned a score of Low for systemic toxicity (single dose) via the inhalation route based on the lack of significant systemic toxicity following single inhalation exposures to the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when negative data, no structural alerts, and no GHS classification are available (CPA 2012a). Amorphous silica (modified) was assigned a score of High for systemic toxicity (single dose) via the oral route based on the changes to the stomach mucosal membrane of animals administered oral doses of the surrogate hexamethyldisilazane at approximately 850 mg/kg. These effects were observed in animals that died prior to and that survived to the scheduled sacrifice, indicating a lack of reversibility. GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (single dose) when effects are observed following single doses of greater than 300 to 2,000 mg/kg (CPA 2012a). Amorphous silica (modified) was assigned a score of Low for systemic toxicity (single dose) via the dermal route based on the lack of a dose-response relationship in the effects observed following dermal application of the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - ECHA 2014
        - *Oral*: In the acute oral toxicity study that identified an oral LD_{50} of 851 mg/kg, poor general condition was observed at approximately 850 mg/kg. Reduced body weights were noted at doses of approximately 850 mg/kg and greater. Gross pathological observations included redness of the stomach mucosal membrane of animals that died prior to the scheduled sacrifice and those that made it to the scheduled sacrifice.
        - *Inhalation:* In the acute inhalation study that identified an inhalation LC_{50} of 10

mg/L, lacrimation, partially closed eyes, inactivity, soft or limp muscles, slow and noisy respiration, body cold to the touch, and soiling around the eyes and urogenital area were observed at 885 ppm (equivalent to 5.84 mg/L[6]). All animals in this concentration group recovered by day 5, with all but one recovering by day 3-4. At 1,167 ppm (equivalent to 7.7 mg/L), the animals exhibited the symptoms identified above in addition to lethargy and labored respiration. The animals in this concentration group that died (50%) exhibited these effects until death, whereas the animals that survived to the scheduled sacrifice recovered by day 5. No clinical signs of toxicity were observed at 3,400 ppm (equivalent to 22.44 mg/L), but all animals died during the latter portion of the 6-hour exposure period. Slight body weight losses were observed in the 1,167 ppm (equivalent to 7.7 mg/L) exposure group animals that survived whereas the body weight increased 12% in the animals exposed to 885 ppm (equivalent to 5.84 mg/L). Congestion of the liver, spleen, and jejunum were observed at 3,400 ppm (equivalent to 22.44 mg/L). Minimal depressed kidney foci were observed in one male at 885 ppm (equivalent to 5.84 mg/L). Pale liver and decreased stomach ingesta were observed in animals that were found dead in the 1,167 ppm (equivalent to 7.7 mg/L) group.

- *Dermal:* In the acute dermal toxicity study that identified a dermal LD_{50} of 547-589 mg/kg, erythema, edema, desquamation, scabs, ecchymosis, and necrosis were observed at dermal doses of 194 mg/kg and higher in females and 387 mg/kg and higher in males. Lethargy, sluggishness, prostration, or other signs of discomfort were also observed at doses of 387 mg/kg and greater in both sexes. Body weights decreased with treatment but it is not clear if the differences were statistically significant. At necropsy, gross pathological findings included darkened lungs and liver and distended bladder filled with red/yellow liquid in males at 774 mg/kg and dark red lungs and trachea in females at 774-3,096 mg/kg. No notable changes were observed in females administered 12,384 mg/kg suggesting a lack of a dose response in these gross pathological observations.

- Surrogate: Silica, amorphous, CAS #7631-86-9
  - EC 2000
    - *Oral*: In most oral toxicity tests no clinical signs of toxicity were observed. Occasional instances of gasping following gavage and colored stools, which was reversible during the observation period, were observed.
    - *Dermal:* Slight erythema and edema were observed following application of silica in acute toxicity studies.
    - *Inhalation:* No clinical signs of toxicity were observed in the acute inhalation studies.

[6] The equivalent concentration in mg/L was calculated using the following equation: mg/L = (ppm x molecular weight)/24,450. The molecular weight of hexamethyldisilazane is 161.395 g/mol.

Group II* Score (repeated dose) **(H, M, or L): H** (inhalation), **L** (oral), DG (dermal)
Amorphous silica (modified) was assigned a score of High for systemic toxicity (repeated dose) via the inhalation route of exposure based on inhalation LOAECs as low as 0.001 mg/L for the surrogate silica, amorphous, in the dust form. GreenScreen® criteria classify chemicals as a High hazard for systemic toxicity (repeated dose) when inhalation LOAECs for dusts are no greater than 0.02 mg/L (CPA 2012a). Amorphous silica (modified) was assigned a score of Low for systemic toxicity (repeated dose) via the oral route of exposure based on NOAELs of 497 to at least 24,200 mg/kg for the surrogate silica, amorphous. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when oral NOAELs/LOAELs are greater than 100 mg/L (CPA 2012a). Amorphous silica (modified) was assigned a score of Data Gap for systemic toxicity (repeated dose) via the dermal route of exposure 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.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - ECHA 2014
        - *Inhalation*: A GLP-compliant repeated dose toxicity study conducted according to OECD 413 was performed with Crl:CD(SD)IGS rats (10/sex/concentration group, additional 10 for control and high concentration recovery groups) administered nose-only inhalation exposures to hexamethyldisilazane (purity not specified) vapor at 0, 0.165, 0.495, or 2.64 mg/L for 6 hours/day, 5 days/week for 13 weeks. The equivalent concentrations for a 7 day/week exposure frequency were 0, 0.118, 0.354, and 1.89 mg/L, respectively. Additional control and high concentration groups were maintained for an additional 4 weeks without treatment. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross pathology, and histopathology. Ataxia and decreased activity were observed in all animals in the high concentration group. Decreased weight gain was observed in high dose males and females but the statistical significance was not specified. Food consumption decreased in high dose males during the entire treatment period and decreased for high dose females during the first two weeks of treatment. Total red blood cells and hematocrit were increased relative to controls in high concentration females at the end of the treatment period. Plasma potassium, sodium, and chloride levels were increased in high concentration females at the end of the treatment period. Urinary pH levels were decreased in high concentration males. High concentration females exhibited increased absolute and relative liver weights. No gross pathological observations were noted with treatment. An increased incidence and severity of increased intra-epithelial hyaline droplets and focal or multifocal basophilic tubules was observed in the kidneys of males of all treatment groups. In the high concentration group, 2/10 males exhibited granular casts were observed in the cortico-medullary junction of the kidneys. The effects to the kidneys of males were considered to be consistent with alpha-2µ-nephropathy which is not relevant for humans. No histopathological changes were observed in the livers of high concentration females to correlate with the changes in liver weights. The study authors identified a NOAEC of 2.64 mg/L (equivalent to 1.89 mg/L for a 7-day/week exposure frequency) based on the lack of treatment-related changes in histopathology that are relevant to humans at up to the highest

concentration tested.

- *Inhalation*: A GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD 422 was performed with Sprague-Dawley rats (10/sex/dose group, additional 10 females for toxicity group) administered whole body inhalation exposures of hexamethyldisilazane (purity not specified) vapor at 0.16, 0.66, or 2.66 mg/L for 6 hours/day for 7 days/week. Females were exposed for 14 days prior to mating, during the mating and gestational periods, and to postnatal days 1-3 for up to 42 days in total. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. Uncoordinated gait and decreased activity were observed immediately following exposure in the high concentration group and persisted for some time following the exposure, but resolved prior to the next day's exposure. A significant decrease in absolute body weights was observed in high concentration females and a decrease in total weight gain was observed in high concentration males and females. Absolute body weights decreased in mid dose females but no significant changes in weight gain were observed for this group. Food consumption decreased in the high concentration males and females. Increased red blood cell counts, hematocrit, and hemoglobin were observed in high concentration females. Decreased plasma glucose and increased cholesterol were observed in high concentration females, and increased cholesterol and sodium levels were observed in high concentration males. Organ weight changes with treatment included decreased lung weights in high concentration females, increased relative kidney weights in mid and high concentration females and high concentration males, and increased relative liver weights in high concentration females. An increased incidence of centrilobular hypertrophy of the liver was observed in high concentration females. No other histopathological findings were noted. The authors identified a NOAEC of 0.66 mg/L and a LOAEC of 2.66 mg/L based on the centrilobular hypertrophy observed in high concentration females.

- Surrogate: Silica, amorphous, CAS #7631-86-9
  - EC 2000
    - *Oral:* Various strains of rats received fumed silica in their feed over periods of time ranging from two weeks to six months. There were no changes seen in any measured parameters. NOAEL values ranged from greater than 497 mg/kg to at least 24,200 mg/kg.
    - *Inhalation, dust*: Numerous studies have been conducted using rats, rabbits, guinea pigs, and monkeys. Studies ranged in length from 2 weeks to 1 year. In all cases, respiratory effects were seen at the lowest doses tested, and no NOAELs could be established from these studies. LOAEL values for these studies would range from less than 0.001 mg/L to less than 0.10 mg/L.
    - *Inhalation, vapor:* Several studies have been conducted using rats, guinea pigs, and rabbits. Studies ranged in length from 12-27 months. In all cases, respiratory effects were seen at the lowest doses tested, and no NOAELs could be established from these studies. It is believed that the NOAELs for repeated dose studies tested via the inhalation route would be below the tested doses.

Neurotoxicity (N)

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

Amorphous silica (modified) was assigned a score of High for neurotoxicity (single dose) based on ToxServices classifying the surrogate hexamethyldisilazane as a GHS Category 2 oral systemic toxicant following single dose. GreenScreen® criteria classify chemicals as a High hazard for neurotoxicity (single dose) when a GHS Category 2 oral systemic toxicity following single dose classification is available (CPA 2012a). The confidence in the score is adjusted as it is not clear if these effects are permanent or reversible. Amorphous silica (modified) was assigned a score of Low for neurotoxicity (single dose) via the inhalation and dermal routes based on the lack of neurotoxic effects observed following single exposures to the surrogates hexamethyldisilazane and silica amorphous. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when negative data, no structural alerts and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014
    - *Oral*: In the acute oral toxicity study that identified an oral LD_{50} of 851 mg/kg, sedation, paralysis of the hind limbs, and anesthesia were observed at approximately 850 mg/kg. No information regarding the reversibility of these effects was presented.
  - Based on neurotoxic effects observed at 851 mg/kg, ToxServices classified hexamethyldisilazane as a GHS Category 2 oral systemic toxicant following single dose for neurotoxicity. GHS Category 2 oral systemic toxicants following single dose cause effects at oral doses of greater than 300 to 2,000 mg/kg (UN 2013).
- Surrogate: Silica, CAS #7631-86-9
  - No data were identified for this endpoint.

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

Amorphous silica (modified) was assigned a score of Low for neurotoxicity (repeated dose) based on no neurotoxic effects observed following inhalation exposures to the surrogate hexamethyldisilazane at up to 2.66 mg/L vapor. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when no neurotoxic effects are observed at vapor concentrations greater than 1.0 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014
    - *Inhalation*: A GLP-compliant combined repeated dose toxicity study with reproduction/developmental toxicity screening test conducted according to OECD 422 was performed with Sprague-Dawley rats (10/sex/dose group, additional 10 females for toxicity group) administered whole body inhalation exposures of

hexamethyldisilazane (purity not specified) vapor at 0.16, 0.66, or 2.66 mg/L for 6 hours/day for 7 days/week. Females were exposed for 14 days prior to mating, during the mating and gestational periods, and to postnatal days 1-3 for up to 42 days in total. The animals were evaluated during the fourth week of exposure in a battery of functional tests that included: hand-held observations, open field observations, categorical observations, rectal temperature, hind-limb/forelimb grip strength, landing foot splay, and motor activity. No treatment-related effects were observed on any of these parameters. ToxServices identified a neurotoxicity NOAEC of 2.66 mg/L based on the lack of neurotoxicity observed at up to the highest concentration tested.

- Surrogate: Silica, amorphous, CAS #7631-86-9
    - No data were identified for this endpoint.

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

Amorphous silica (modified) was assigned a score of Low for skin sensitization based on negative results for skin sensitization in a guinea pig maximization test. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when negative results, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
    - Evonik 2010
        - Amorphous silica (modified) was not sensitizing to the skin of guinea pigs in a maximization test conducted according to OECD 406. No further details were provided.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - No data were identified for this endpoint.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - EC 2000
        - In a guinea pig maximization test conducted according to Directive 84/449/EEC, B.6 "Acute toxicity (skin sensitization)," chemically prepared silica (CAS 7631-86-9) was found to be non-sensitizing (no further details available).

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

Amorphous silica (modified) 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.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - No data were identified for this endpoint.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - No data were identified for this endpoint.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for skin irritation/corrosivity based on it not being irritating to the skin. 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 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - Evonik 2010
    - Amorphous silica (modified) was not irritating to the skin of rabbits in an OECD 404 test. No further details were provided.
  - Cabot 2007
    - Amorphous silica (modified) was not irritating to the skin based on a dermal irritation score of 0/8. No further details were provided.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - Screening lists
    - GHS New Zealand Category 8.2C (equivalent to GHS Category 1 eye irritant) corrosive to dermal tissue
      - Based on R-phrase from company data.
  - ECHA 2014
    - A GLP-compliant dermal irritation test conducted according to OECD 404 was performed with New Zealand White rabbits (three total, sex not specified) administered topical applications of 0.5 mL undiluted hexamethyldisilazane (purity not specified) to shaved skin under semi-occlusive dressing for 4 hours. The animals were observed for 1, 24, 48, and 72 hours and 7 days. The primary dermal irritation index (PDII) was 1.22/8 and the dermal irritation effects were fully reversible within 7 days. Erythema was observed at 24, 48, and 72 hours in 2/3 rabbits. The third animal exhibited no signs of irritation during the study. The study authors concluded that hexamethyldisilazane was not irritating to the skin in this study.
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - EC 2000
    - Silica was not irritating to the eyes in a series of ocular irritation tests performed with rabbits.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for eye irritation/corrosivity based on it not being irritating to the eyes of rabbits. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when negative data, no structural alerts, and no GHS classification are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - Evonik 2010
    - Amorphous silica (modified) was not irritating to the eyes of rabbits in an OECD 405 test. No further details were provided.
  - Cabot 2007

        - Amorphous silica (modified) was not irritating to the eyes based on a Draize score of 0.0/110 at 24 hours. No further details were provided.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - Screening lists:
        - GHS New Zealand Category 8.3A (equivalent to GHS Category 1 skin irritant) corrosive to ocular tissue
            - Based on R-phrase from company data.
    - ECHA 2014
        - A GLP-compliant ocular irritation study conducted according to OECD 405 was performed with New Zealand White rabbits (3 total, sex not identified) administered ocular instillations of 0.1 mL undiluted hexamethyldisilazane (purity not specified) without washing. The animals were observed for 72 hours. A mean overall Draize irritation score of 0 was calculated for this study and the authors concluded that hexamethyldisilazane was not irritating to the eyes.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - EC 2000
        - Silica was not irritating to the skin in a series of dermal irritation tests performed with rabbits.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
Amorphous silica (modified) was assigned a score of Low for acute aquatic toxicity based on the acute aquatic toxicity values of 10,000 mg/L for fish and daphnia and greater than 10,000 mg/L for green algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 100 mg/L (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
    - Cabot 2007
        - 96-hour NOEC (*Danio rerio*, zebrafish) = 10,000 mg/L (OECD 203)
        - 24-hour NOEC (*Daphnia magna*) = 10,000 mg/L (OECD 202)
        - 72-hour growth inhibition EC_{50} (green algae) = greater than 10,000 mg/L (OECD 2010)
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - ECHA 2014
        - A GLP-compliant OECD 111 hydrolysis test identified a hydrolysis half-life of up to 30 seconds at pH 7. Therefore, it is highly likely that the aquatic biota used in the acute aquatic toxicity tests were exposed to the hydrolysis products, not hexamethyldisilazane.
        - 96-hour LC_{50} (*Danio rerio*, zebrafish) = 88 mg/L (GLP-compliant, EU Method C.1)
        - 48-hour EC_{50} (*Daphnia magna*) = 80 mg/L (GLP-compliant, EU Method C.1)
        - 72-hour growth rate EC_{50} (*Desmodesmus subspicatus*, green algae) = 50 mg/L (GLP-compliant, EU Method C.3)
        - 72-hour biomass EC_{50} (*Desmodesmus subspicatus*, green algae) = 19 mg/L (GLP-compliant, EU Method C.3)
- Surrogate: Silica, amorphous, CAS #7631-86-9

- EC 2000
  - 96-hour LC_{50} (*Brachydanio rerio*, zebrafish) = 5,000 mg/L (as chemically prepared silica (CAS #7631-86-9))
  - 48-hour EC_{50} (*Ceriodaphnia dubia*, water flea) = 7,600 mg/L (as chemically prepared silica (CAS #7631-86-9))
  - 72-hour EC_{50} (*Selenastrum capricornutum*) = 440 mg/L ((as chemically prepared silica (CAS #7631-86-9); ISO 8691 "Water quality – fresh water algal growth inhibition test with *Scenedesmus subspicatus* and *Selenastrum capricornutum*")

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): M
Amorphous silica (modified) was assigned a score of Moderate for chronic aquatic toxicity based on chronic aquatic toxicity values of 2.7-7.5 mg/L for the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a Moderate hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 1 to 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014
    - A GLP-compliant OECD 111 hydrolysis test identified a hydrolysis half-life of up to 30 seconds at pH 7. Therefore, it is highly likely that the aquatic biota used in the chronic aquatic toxicity tests were exposed to the hydrolysis products, not hexamethyldisilazane.
    - 72-hour growth rate NOEC (*Desmodesmus subspicatus*, green algae) = 7.5 mg/L (GLP-compliant, EU Method C.3)
    - 72-hour biomass NOEC (*Desmodesmus subspicatus*, green algae) = 2.7 mg/L (GLP-compliant, EU Method C.3)
- Surrogate: Silica, amorphous, CAS #7631-86-9
  - No data identified for this endpoint.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *vH*
Amorphous silica (modified) was assigned a score of Very High for persistence based on the surrogates hexamethyldisilazane and silica, amorphous, being listed on screening lists. GreenScreen® criteria classify chemicals as a High to Very High hazard for persistence when they are listed on Environment Canada's Domestic Substance List (DSL) as persistent (CPA 2012a). ToxServices assigned a Very High score for this endpoint in order to be protective of human health. The confidence in the score is adjusted as it is based on a screening list.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists for this endpoint.
  - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
  - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
  - ECHA 2014

        - A GLP-compliant ready biodegradability test conducted according to EU C.4E (Closed Bottle test) was performed with activated domestic sludge (adaptation not specified) exposed to hexamethyldisilazane (purity not specified) at 2 mg/L for 28 days. At the end of the exposure period, the level of degradation was 15.3%. The study authors concluded that hexamethyldisilazane was not readily biodegradable in this study.
    - Screening lists:
        - Environment Canada Domestic Substance List (DSL) – persistent
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - Screening lists:
        - Environment Canada Domestic Substance List (DSL) – persistent
    - EC 2000
        - Biodegradation is not expected as silica is an inorganic chemical.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
Amorphous silica (modified) was assigned a score of Very Low for bioaccumulation based on a predicted BCF of 42.61 and an estimated log K_{ow} of 2.62 for the surrogate hexamethyldisilazane. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when log K_{ow} values are no greater than 4 and BCF values are no greater than 100 (CPA 2012a). The confidence in the score is adjusted as it is based on modeling.

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - U.S. EPA 2012
        - Hexamethyldisilazane is predicted to have a log K_{ow} of 2.62.
        - BCFBAF predicts a BCF of 42.61 based on an estimated log K_{ow} of 2.62.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - EC 2000
        - Bioaccumulation is not expected as silica is an inorganic chemical.
        - Silica is not expected to be soluble in octanol.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Amorphous silica (modified) was assigned a score of Low for reactivity based on the surrogate hexamethyldisilazane not being considered explosive or oxidizing. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when negative data and no GHS classification are available (CPA 2012a). The confidence in this score is adjusted as it is not based on data or 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.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - ECHA 2014

        - Hexamethyldisilazane is described as non-explosive and non-oxidizing in the secondary literature.
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - No data were identified for this endpoint.

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

Amorphous silica (modified) was assigned a score of Low for flammability based on amorphous silica not being flammable. GreenScreen® criteria classify chemicals as a Low hazard for flammability when no GHS classifications for flammability are available (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists for this endpoint.
    - *Screening:* Not listed on any screening lists for this endpoint.
- Amorphous silica (modified), CAS #68909-20-6
    - No data were identified for this endpoint.
- Surrogate: Hexamethyldisilazane, CAS #999-97-3
    - Screening lists:
        - GHS New Zealand Category 3.1B (equivalent to GHS Category 2 flammable liquid) – flammable liquids: high hazard
            - Based on R-phrase from company data.
    - ECHA 2014
        - Hexamethyldisilazane has a flash point of 11.4°C at 1,013 hPa in a non-GLP-compliant closed cup test conducted according to EU Method A.9.
        - Hexamethyldisilazane has a boiling point of 125°C at 1,013 hPa.
    - Based on these results ToxServices classified hexamethyldisilazane as a GHS Category 2 flammable liquid. GHS Category 2 flammable liquids have flash points less than 23°C and an initial boiling point of greater than 35°C (UN 2013).
- Surrogate: Silica, amorphous, CAS #7631-86-9
    - EC 2000
        - Silica is non-flammable.

References

Cabot. 2007. Safety Data Sheet for CAB-O-SIL® TS-530, TS-530D (CAS #68909-20-6). Revision date October 31, 2007. Available at: http://www.cabot-corp.com/wcm/msds/en-gb/FS/TS530D-EUR-EN.pdf.

Chemical Carcinogenesis Research Information System (CCRIS). 2008. Entry for silicon dioxide (CAS #7631-86-9). United States National Library of Medicine. Available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS.

ChemIDplus. 2014. Entry for Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica (CAS #68909-20-6). United States National Library of Medicine. Available at: http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp.

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

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

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

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

European Chemicals Agency (ECHA). 2014. REACH Dossier for 1,1,1,3,3,3-Hexamethyldisilazane (CAS #999-97-3). Available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eaa4137-0deb-68e3-e044-00144f67d031/DISS-9eaa4137-0deb-68e3-e044-00144f67d031_DISS-9eaa4137-0deb-68e3-e044-00144f67d031.html.

European Commission (EC). 2000. IUCLID Dataset for Silicon dioxide, chemically prepared (CAS #7631-86-9). European Commission Joint Research Centre. Available at: http://esis.jrc.ec.europa.eu/doc/IUCLID/datasheet/7631869.pdf.

Evonik. 2010. Safety Data Sheet for Aérosol® R 812 S (CAS#68909-20-6). Version 1.18. Revision date May 31, 2010. Available at: http://www.stobec.com/documents/msds/8070.pdf.

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

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

Pharos. 2014. Pharos Chemical and Material Library Entry for Hexamethyldisilazane Treated Silica Dioxide (CAS #68909-20-6). Available at: http://www.pharosproject.net/material/.

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

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

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available at: http://www.gpo.gov/fdsys/pkg/CFR-2008-title49-vol2/pdf/CFR-2008-title49-vol2-sec172-101.pdf.

United States Department of Transportation (U.S. DOT). 2008b. Classification Criteria. 49 CFR § 173. Available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title49/49cfr173_main_02.tpl.

United States Environmental Protection Agency (U.S. EPA). 2012. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available at: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

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 Amorphous Silica (Modified) (CAS #68909-20-6)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector for Inhalation Exposure

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	**Amorphous silica (modified)**	**68909-20-6**	**L**	**L**	**L**	**L**	DG	**vH**	**L**	**H**	**L**	**L**	**L**	DG	**L**	**L**	**L**	**M**	*vH*	*vL*	*L*	**L**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Amorphous silica (modified)	1

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Amorphous silica (modified)	1

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												1
2												
3												
4												

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector for Oral Exposure

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	**Amorphous silica (modified)**	**68909-20-6**	**L**	**L**	**L**	**L**	DG	**L**	**H**	**L**	**H**	**DG**	**L**	DG	L	L	**L**	**M**	*vH*	*vL*	*L*	**L**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Amorphous silica (modified)	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Amorphous silica (modified)	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												

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector for Dermal Exposure

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	**Amorphous silica (modified)**	**68909-20-6**	**L**	**L**	**L**	**L**	DG	**H**	**L**	DG	**L**	DG	**L**	DG	**L**	**L**	**L**	**M**	*vH*	*vL*	*L*	**L**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Amorphous silica (modified)	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Amorphous silica (modified)	U

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	No	Yes	Yes	Yes							U
3												
4												

APPENDIX C: Pharos Output for Amorphous Silica (Modified) (CAS #68909-20-6)

HEXAMETHYLDISILAZANE TREATED SILICA DIOXIDE

CAS RN: 68909-20-6

Synonyms: Hexamethyldisilazane, silica reaction product; Methylsilylated Silica; Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica

Direct Chemical and Compound Hazard Quickscreen — Detailed Hazard Listings

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

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

APPENDIX D: Pharos Output for Hexamethyldisilazane (CAS #999-97-3)

HEXAMETHYLDISILAZAN

CAS RN: 999-97-3

Synonyms: 1,1,1,3,3,3-HEXAMETHYLDISILAZANE

Detailed Direct Hazard Listings — Quickscreen

EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 8.3A - Corrosive to ocular tissue - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 8.2C - Corrosive to dermal tissue - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	New Zealand HSNO/GHS (GHS-New Zealand) 3.1B - Flammable Liquids: high hazard - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (dermal) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (inhalation) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
TERRESTRIAL	New Zealand HSNO/GHS (GHS-New Zealand) 9.3C - Harmful to terrestrial vertebrates - Not included in GreenScreen
PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified (LT-U)
RESTRICTED LIST	German FEA - Substances Hazardous to Waters (VwVwS) Class 1 Low Hazard to Waters - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only

Compound Group Hazard Listings

APPENDIX E: Pharos Output for Silica, Amorphous (CAS #7631-86-9)

SILICA, AMORPHOUS

CAS RN: 7631-86-9

Synonyms: Silicon dioxide; Silica Dioxide; Diatomaceous earth; Diatomaceous silica; Siliceous earth; Silica gel

Detailed Direct Hazard Listings — Quickscreen

CANCER	US CDC - Occupational Carcinogens (NIOSH-C) Occupational carcinogen - GreenScreen Benchmark 1 (LT-1) - occupational hazard only - HPD
CANCER	Intnl Agency for Rsrch on Cancer - Cancer Monographs (IARC) Group 3: Agent is not classifiable as to its carcinogenicity to humans - GreenScreen Benchmark Unspecified (LT-U)
PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified (LT-U)
EXEMPT	German FEA - Substances Hazardous to Waters (VwVwS) Non-Hazardous to Water (Water Hazard Class 0 NWG) - Not included in GreenScreen

Compound Group Hazard Listings

APPENDIX F: EPISuite Modeling Results for Hexamethyldisilazane (CAS #999-97-3)

CAS Number: 999-97-3
SMILES: C[Si](N[Si](C)(C)C)(C)C
CHEM: Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-
MOL FOR: C6 H19 N1 Si2
MOL WT: 161.40
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log K_{ow} (octanol-water): ------
Boiling Point (deg C): ------
Melting Point (deg C): -76.20
Vapor Pressure (mm Hg): 18
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) = 2.62

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 107.63 (Adapted Stein & Brown method)
Melting Pt (deg C): -58.07 (Mean or Weighted MP)
VP (mm Hg,25 deg C): 12.5 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 1.67E+003 (Mean VP of Antoine & Grain methods)
BP (exp database): 125 deg C
VP (exp database): 1.38E+01 mm Hg (1.84E+003 Pa) at 25 deg C

Water Solubility Estimate from Log K_{ow} (WSK_{ow} v1.42):
Water Solubility at 25 deg C (mg/L): 761
log K_{ow} used: 2.62 (estimated)
melt pt used: -76.20 deg C

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 7.8558 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 8.69E-005 atm-m^3/mole (8.81E+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: 5.023E-003 atm-m^3/mole (5.090E+002 Pa-m^3/mole)
VP: 18 mm Hg (source: User-Entered)
WS: 761 mg/L (source: WSK_{ow}WIN)

Log Octanol-Air Partition Coefficient (25 deg C) [K_{oa}WIN v1.10]:
Log K_{ow} used: 2.62 (K_{ow}Win est)
Log K_{aw} used: -2.449 (HenryWin est)
Log K_{oa} (K_{oa}WIN v1.10 estimate): 5.069
Log K_{oa} (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.6707
Biowin2 (Non-Linear Model): 0.6719
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.8425 (weeks)
Biowin4 (Primary Survey Model): 3.6149 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.2345
Biowin6 (MITI Non-Linear Model): 0.1174
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.3587
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): 2.4E+003 Pa (18 mm Hg)
Log K_{oa} (K_{oa}win est): 5.069
Kp (particle/gas partition coef. (m^3/µg)):
Mackay model: 1.25E-009
Octanol/air (K_{oa}) model: 2.88E-008
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model: 4.51E-008
Mackay model: 1E-007
Octanol/air (K_{oa}) model: 2.3E-006

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 0.8976 E-12 cm^3/molecule-sec
Half-Life = 11.916 Days (12-hr. day; 1.5E6 OH/cm^3)
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
7.26E-008 (Junge-Pankow, Mackay avg)
2.3E-006 (K_{oa} method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 340.7 L/kg (MCI method)
Log K_{oc}: 2.532 (MCI method)
K_{oc}: 187.7 L/kg (K_{ow} method)
Log K_{oc}: 2.273 (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 = 1.394 (BCF = 24.77 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 0.3241 days (HL = 2.109 days)
Log BCF Arnot-Gobas method (upper trophic) = 1.630 (BCF = 42.61)
Log BAF Arnot-Gobas method (upper trophic) = 1.630 (BAF = 42.62)
log K_{ow} used: 2.62 (estimated)

Volatilization from Water:
Henry LC: 8.69E-005 atm-m^3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 9.856 hours
Half-Life from Model Lake: 214 hours (8.919 days)

Removal In Wastewater Treatment:
Total removal: 7.63 percent
Total biodegradation: 0.10 percent
Total sludge adsorption: 3.28 percent
Total to Air: 4.24 percent
(using 10000 hr. Bio P,A,S)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr.)	Emissions (kg/hr.)
Air	7.08	286	1000
Water	21.8	360	1000
Soil	70.8	720	1000
Sediment	0.314	3.24e+003	0

Persistence Time: 455 hr.

Sources to Check for GreenScreen® Hazard Assessment

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

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

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

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

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

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

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

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

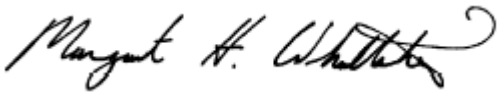
European Chemicals Agency (ECHA) REACH Dossiers: http://echa.europa.eu/

Licensed GreenScreen® Profilers

Amorphous Silica (Modified) GreenScreen® Evaluation Prepared by:

Zach Guerrette, Ph.D.
Toxicologist
ToxServices LLC

Amorphous Silica (Modified) GreenScreen® Evaluation QC'd by:



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