

GRAPHENE (PROPHENE™ PS100)
(CAS #1034343-98-0)
GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: July 8, 2025

ToxServices Review Date: July 8, 2030¹



¹ Although CPA's Assessment Expiration Policy (CPA 2018a) indicates that Benchmark 1 assessments have no expiration date, ToxServices strives to review BM-1s in a five-year period to ensure currency of data presented in the BM-1 GreenScreen® assessments.

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GreenScreen® Executive Summary for Graphene (Prophene™ PS100)

Graphene is a type of carbon nanomaterial. It is a two-dimensional form of graphite consisting of layers of single atom thick sheets of carbon crystallized as a honeycomb structure monolayer. Graphene is categorized into three types based on the number of carbon layers (L) stacked: monolayer graphene (1 L), few-layer graphene (FLG) (<5 L), and multilayer graphene (MLG) (<10 L), with each type having its own physical properties that influence their industrial applications.

This GreenScreen® assessment is for graphene with the trade name of Prophene™ PS100. It is an FLG (number of layers < 15, but total mono-, bi-, and tri-layer content is > 70%), with a surface area not greater than 180 m²/g, a carbon content greater than 99% and an oxygen content less than 1%. The lateral particle size is between 100 nm to 5 µm with particle thickness of less than 2 nm. Prophene™ PS100 is a black crystalline powder that is insoluble in water. It is neither flammable nor reactive.

Graphene (Prophene™ PS100) was assigned a **GreenScreen Benchmark™ Score of 1** (“Avoid—Chemical of High Concern”). This score is based on the following hazard score combination:

- Benchmark 1b
 - Very High Persistence-P + Very High Ecotoxicity (chronic aquatic toxicity-CA)

Data gaps (DG) exist for carcinogenicity-C, endocrine activity-E, systemic toxicity (repeated dose)-STr*, and neurotoxicity (repeated dose)-Nr*. As outlined in GreenScreen® Guidance, Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), graphene (Prophene™ PS100) meets requirements for a GreenScreen Benchmark™ Score of 1 despite the hazard data gaps. In a worst-case scenario, if graphene (Prophene™ PS100) were assigned a High score for the data gaps C, E, STr*, or Nr*, it would still be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in vitro* tests for genotoxicity, skin and eye irritation, and ECHA’s expert guidance on the evaluation of respiratory sensitization. The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties:

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

No Type I (input data) uncertainties on using graphene (Prophene™ PS100)’s NAMs dataset (*in vitro* genotoxicity, skin and eye irritation tests) are identified. Graphene (Prophene™ PS100)’s Type II (extrapolation output) uncertainties include the limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions, uncertain applicability of the bacterial reverse mutation assay to testing nanomaterials, the limitation of the *in vitro* skin corrosion test (OECD TG 439) to identify substances classified as mild skin irritant (GHS Category 3), the limitation of the *in vitro* eye irritation test (OECD TG 492) to differentiate between Category 2 and Category 1, or between Category 2A and Category 2, lack of consideration of non-immunological mechanisms of respiratory sensitization, and the uncertainty regarding the applicability of ECHA’s guidance on respiratory sensitization to inorganics and nanomaterials. Some of the type I and type II errors can be alleviated by the use of genotoxicity test batteries in combination with *in vivo* data for skin and eye irritation as there are no validated *in vitro* methods available for the direct identification of Category 2 eye irritants and Category 3 skin irritants, and ECHA’s decision framework to evaluate respiratory sensitization.

GreenScreen® Hazard Summary Table for Graphene (Prophene™ PS100)

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

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after “repeat” for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

**GreenScreen® Chemical Assessment for Graphene (Prophene™ PS100)
(CAS #1034343-98-0)**

Method Version: GreenScreen® Version 1.4

Assessment Type²: Certified

Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment (v.1.4) Prepared By:

Name: Mouna Zachary, Ph.D.

Title: Senior Toxicologist

Organization: ToxServices LLC

Date: March 21, 2025; June 30, 2025

Quality Control Performed By:

Name: Bingxuan Wang, Ph.D., D.A.B.T.

Title: Senior Toxicologist

Organization: ToxServices LLC

Date: March 24, 2025; July 8, 2025

ToxServices Review Date: July 8, 2025, 2030³

Chemical Name: Graphene (Tradename Prophene™ PS100).

CAS Number: Graphene is a type of carbon nanomaterial and is categorized into three types based on the number of carbon layers (L) stacked: monolayer graphene (1 L), few-layer graphene (FLG) (<5 L), and multilayer graphene (MLG) (<10 L), with each type having its own physical properties as shown in Figure 1. The CAS 1034343-98-0 refers to all types of graphene.

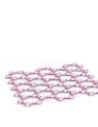
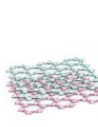
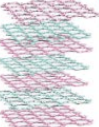

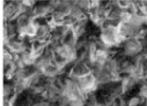

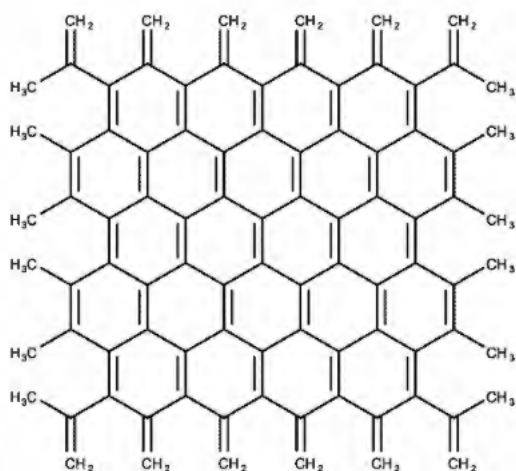
	Graphene & derivatives			Graphite & derivatives		
Type of graphene						
	SLG	FLG	MLG	Nanoplates/ nanosheets	Microplates/ microsheets	Graphite powders
Number of layers	1	2-5	< 10	< 250	< 250000	< 1 million
Maximal thickness	< 1nm	1nm	3nm	< 100nm	< 10µm	> 100µm

Figure 1: Graphene Types and Properties (Carbon Waters 2025)

Chemical Structure(s): Graphene is a carbon nanomaterial and is a two-dimensional form of graphite consisting of layers of single atom thick sheets of carbon crystallized as a honeycomb structure monolayer. A single layer of carbon atoms arranged in such a honeycomb structure forms a single graphene sheet (SLG). Several sheets stacked one on top of the other are regarded as few layer graphene (FLG) or multi-layer graphene (MLG, usually less than 30 layers). The tradename Prophene™ PS100 contains < 15 layers, and >70% mono-, bi-, and tri-layers combined (Akron Polymer Solutions 2025). A representative chemical structure for graphene is shown below:

² GreenScreen® reports are either “UNACCREDITED” (by unaccredited person), “AUTHORIZED” (by Authorized GreenScreen® Practitioner), or “CERTIFIED” (by Licensed GreenScreen® Profiler or equivalent).

³ Although CPA’s Assessment Expiration Policy (CPA 2018a) indicates that Benchmark 1 assessments have no expiration date, ToxServices strives to review BM-1s in a five-year period to ensure currency of data presented in the BM-1 GreenScreen® assessments.



Structure for graphene (AICIS 2023) (ECHA, CAS #1034343-98-0, 2025)

Also called: Single and multilayer turbostratic graphene; Graphene Flower; Graphene nanoplatelets; Graphenes (PubChem 2025).

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):

This GreenScreen® assessment is for graphene with the trade name of Prophene™ PS100. Due to differences in manufacturing processes, graphene based materials vary widely in their physiochemical properties which may affect their potential toxicity. The most important physicochemical characteristics that influence toxicity of graphene are surface area, particle size (lateral size and thickness), number of layers, surface modification, and aggregation.

Prophene™ PS100 is a FLG (number of layer < 15, but total mono-, bi-, and tri-layers > 70%), with a surface area not greater than 180 m²/g, a carbon content greater than 99% and an oxygen content less than 1%. The lateral particle size is 100 nm-5 µm with particle thickness of less than 2 nm (Akron Polymer Solutions 2025). Prophene™ PS100 contains > 99% carbon, < 0.5% water, and < 1% oxygen (Akron Polymer Solutions 2025). Thus, ToxServices considered Prophene™ PS100 to be an FLG that is non-functionalized. No toxicity data specific to Prophene™ PS100 were identified. The Australian Industrial Chemicals Introduction Scheme (AICIS) evaluated two commercial grades/forms of graphene multilayer powder (ML-100 and XE) with similar physical properties to Prophene™ PS100 (smaller particle size 6-100 nm, 99% carbon, surface area < 180 m²/g, and no surface modification). The AICIS considered data on other non-modified graphene particles (ML, FL, and SL) with various dimensions to fill data gaps. ToxServices therefore also considered data on these graphene types in this assessment. In addition, ToxServices identified a RAECH dossier for graphene nanoform (lateral dimension: 700 - 2,000 nm and surface area of ≥ 7 and ≤ 750 m²/g) and considered its data to fill the data gaps. The AICIS also included data on this type of graphene in its assessment.

As all types of graphene are associated with the same CAS and have the same chemical structure, ToxServices considered them representative of the target chemical. However, the confidence level of the score is reduced only for aquatic toxicity and systemic toxicity related endpoints when it is based on data for different graphene types with varying particle sizes. In contrast, available data indicate that the irritation and sensitization potential of graphene based materials depends on factors such as surface chemistry, and purity rather than particle size. Therefore, non-modified graphene types with different

particle sizes can serve as representatives for assessing the irritation and sensitization potential Prophene™ PS100 and the confidence level would be high. For the flammability endpoint, ToxServices considered data on graphite (CAS #7782-42-5) as supporting data. Graphite is also an inorganic form of carbon with layered hexagonal sheets.

Identify Applications/Functional Uses:

Thermal conductor and used as an additive in industrial coolants, lubricants, diesel fuels, and as a component of thermal coatings and batteries (Akron Polymer Solutions 2025, AICIS 2023).

Known Impurities⁴:

Prophene™ PS100 contains > 99% carbon, < 0.50% moisture, < 1.0% oxygen, and ~ 0.50% ash (Akron Polymer Solutions 2025).

GreenScreen® Summary Rating for Graphene (Prophene™ PS100)^{5,6 7,8}: Graphene (Prophene™ PS100) was assigned a **GreenScreen Benchmark™ Score of 1** (“Avoid—Chemical of High Concern”) (CPA 2018b). This score is based on the following hazard score combination:

- Benchmark 1b
 - Very High Persistence-P + Very High Ecotoxicity (chronic aquatic toxicity-CA)

Data gaps (DG) exist for carcinogenicity-C, endocrine activity-E, systemic toxicity (repeated dose)-STr*, and neurotoxicity (repeated dose)-Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), graphene (Prophene™ PS100) meets requirements for a GreenScreen Benchmark™ Score of 1 despite the hazard data gaps. In a worst-case scenario, if graphene (Prophene™ PS100) were assigned a High score for the data gaps C, E, STr*, or Nr*, it would still be categorized as a Benchmark 1 Chemical.

Figure 2: GreenScreen® Hazard Summary Table for Graphene (Prophene™ PS100)

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

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after “repeat” for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

⁴ Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.

⁵ For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

⁶ See Appendix A for a glossary of hazard endpoint acronyms.

⁷ For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).

⁸ For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

Environmental Transformation Products

No transformation products were identified, as Prophene™ PS100 is an inorganic nanomaterial that is persistent in the environment. Graphene, regardless of form, is composed essentially of carbon which is ubiquitous in the environment.

Introduction

Prophene™ PS100 is a multilayer graphene powder with a surface area not greater than 180 m²/g, a carbon content greater than 99% and an oxygen content less than 1%. The lateral particle size is between 100 nm to 5 µm. It is used in several industrial applications to enhance electrical conductivity, thermal management, mechanical strength, anti-corrosion, lubrication, and anti-wear (Akron Polymer Solutions 2025). In general, graphene is a carbon nanomaterial and is isolated from crystalline graphite through two methods: chemical vapor deposition (bottom up method) or exfoliation of natural graphite (chemical, mechanical, oxidative, top down method) (Carbon Waters 2025). Because of its unique structural, specific surface area and mechanical characteristics, it is used in several industrial applications such as energy storage; nanoelectronic devices and batteries (Carbon Waters 2025).

ToxServices assessed graphene (Prophene™ PS100) against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2021).

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

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2025). It can be accessed at: <http://www2.epa.gov/saferchoice/safer-ingredients>. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2024).

Graphene is not listed on the SCP SCIL.

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 2018b). Pharos (Pharos 2025) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),⁹ which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for graphene can be found in Appendix C.

- Graphene is an LT-U chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Graphene is not listed on the U.S. DOT list.
- Graphene is not on any GreenScreen®-specified lists.

Hazard Statement and Occupational Control

No Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements specific to Prophene™ PS100 was identified. Graphene (unspecified type) is associated with one GHS

⁹ DOT lists are not required lists for GreenScreen® List Translator v1.4. They are reference lists only.

hazard statement, as shown in Table 1, identified by the authors of its REACH registration dossier and the majority of notifiers (ECHA CHEM, CAS #1034343-98-0, 2025, PubChem 2025). General personal protective equipment (PPE) recommendations, and occupational exposure limits (OELs) are presented in Table 2.

Table 1: GHS H Statements for Graphene (CAS #1034343-98-0) (PubChem 2025, ECHA CHEM, CAS #1034343-98-0, 2025)	
H Statement	H Statement Details
H412	Harmful to aquatic life with long lasting effects.

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Graphene (CAS #1034343-98-0)			
Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Wear eye protection, protective gloves, protective clothing, respiratory protection	Enerage 2024	TWA/TLV: 2.0 mg/m ³ (U.S ACGIH)	Enerage 2024
		TWA /REL: 2.5 mg/m ³ (U.S. NIOSH)	
		TWA: 15 mg/m ³ for the total dust and respirable fraction of elemental carbon (U.S. OSHA)	
TWA: Time Weighted Average TLV: Threshold Limit Value ACGIH: American Conference of Governmental Industrial Hygienists REL: Recommended Exposure Limits NIOSH: National Institute for Occupational Safety and Health OSHA: Occupational Safety and Health Administration			

Physicochemical Properties of Graphene (Prophene™ PS100)

Prophene™ PS100 is a black crystalline powder that is insoluble in water. Due to differences in manufacturing processes, graphene materials vary widely in their physiochemical properties which may affect their potential toxicity. The most important physicochemical characteristics that influence the toxicity of graphene are number of layers, particle size, agglomeration/aggregation, surface properties (area, charge, defects, coating, reactivity), impurities, and density. These properties have been previously described for Prophene™ PS100. Table 3 lists the other physicochemical properties for graphene.

Table 3: Physical and Chemical Properties of Graphene (CAS #1034343-98-0)		
Property	Value	Reference
Molecular formula	C	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023
SMILES Notation	[C]	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023
Molecular weight	12	ECHA CHEM, CAS

Table 3: Physical and Chemical Properties of Graphene (CAS #1034343-98-0)		
Property	Value	Reference
		#1034343-98-0, 2025; AICIS 2023
Physical state	Solid, nanomaterial form	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023
Appearance	Black powder	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023, Akron Polymer Solutions 2025
Melting point	4,000°C (estimated based on data for graphite) > 3,600°C	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023; Enerage 2024
Boiling point	Not conducted as the melting point of the test substance is > 300°C	ECHA CHEM, CAS #1034343-98-0, 2025
Vapor pressure	Not available	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023
Water solubility	< 100 ppb (insoluble)	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023
Dissociation constant	Not available	
Density/specific gravity	True density = 2.2 g/cm ³ (non-GLP study, ASTM D 5550)	ECHA CHEM, CAS #1034343-98-0, 2025; AICIS 2023, Akron Polymer Solutions 2025
Partition coefficient	Not applicable, as substance is inorganic	
Particle size	Prophene™ PS100: 100 nm to 5 µm	Akron Polymer Solutions 2025
Structure	Two-dimensional, carbon layers/sheets, Hexagonal	Akron Polymer Solutions 2025, AICIS 2023
Bioavailability	Graphene is not absorbed through skin and is not expected to have high systemic absorption through the gastrointestinal tract and inhalation routes. However, due to lack of data, ECHA dossier authors conservatively assumed that graphene was bioavailable by the oral and inhalation routes	ECHA CHEM, CAS #1034343-98-0, 2025

Toxicokinetics

No toxicokinetic data are available for graphene. In general, graphene nanoparticles (GNPs) are highly stable and chemically unreactive; therefore, absorption and metabolism in the body are not major concerns. The primary toxicokinetic considerations for GNPs are distribution and clearance in the respiratory tract. In addition, the absorption, distribution, and excretion of graphene nanoparticles may

be affected by various factors including the administration routes, physicochemical properties, particle agglomeration and surface coating of GFNs. Authors of REACH dossier for a non-modified graphene nanoparticle with lateral dimension of 700 -2,000 nm and surface area of ≥ 7 and ≤ 750 m²/g made the following toxicokinetic assumptions based on its physical chemical properties.

- Absorption
 - ECHA CHEM, CAS #1034343-98-0, 2025
 - Oral and inhalation absorption of GNPs are not significant based on the results from acute toxicity studies in rats. However, the authors of REACH dossier conservatively assumed 100% absorption for these routes of exposures. An absorption rate of 10% was assumed for the dermal route of exposure.
- Distribution
 - ECHA CHEM, CAS #1034343-98-0, 2025
 - GNPs are expected to deposit in the lung and remain within the lungs for up to three months as indicated in several studies when administered by inhalation or intratracheal instillation.
- Metabolism
 - No data available.
- Excretion
 - ECHA CHEM, CAS #1034343-98-0, 2025
 - GNPs are expected to be excreted unchanged via the feces. This also applies to the inhaled particles when swallowed.
- In summary, oral and inhalation absorption of GNPs are assumed to be high (100%). In contrast, dermal absorption is assumed to be low. GNPs are expected to deposit in the lung and remain within the lungs for up to three months. The main excretion pathway for GNPs is expected to be via feces.

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Graphene (Prophene™ PS100) was assigned a score of Data Gap for carcinogenicity based on lack of data for this endpoint.

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

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

Graphene (Prophene™ PS100) was assigned a score of Low for mutagenicity/genotoxicity based on negative results in *in vitro* and *in vivo* genotoxicity and clastogenicity assays with nanoform graphene containing respirable particles. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on measured data from different graphene types with varying particle sizes.

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

- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - *In vitro*: Graphene (nano platelet) was negative for clastogenicity in a GLP-compliant chromosome aberration assay conducted according to OECD Technical Guideline (TG) 473 in which human peripheral blood lymphocytes cells were exposed to the test substance in aqueous 0.1% (w/v) carboxymethylcellulose sodium at concentrations up to 2,000 µg/mL with and without metabolic activation. There were no significant increases in chromosome aberrations reported under the conditions of this assay. Vehicle control and positive controls (cyclophosphamide and mitomycin C) were reported as valid. However, the study authors noted that there was no evidence that the test substance was able to enter the cells (Klimisch 1, reliable without restriction).
 - *In vitro*: Negative results for mutagenicity were obtained in a GLP-compliant mammalian cell gene mutation test conducted according to OECD TG 476 with graphene (nano platelet). Chinese hamster lung fibroblasts (V79) cells were exposed to the test substance at concentrations of 0.002 to 0.5 µg/mL for 4 hours with and without metabolic activation (S9 mix). No cytotoxicity and no increase in the mutation frequency was found at any of the tested dose levels. Vehicle and positive controls were reported as valid (Klimisch 1, reliable without restriction).
 - *In vivo*: In a GLP-compliant combined *in vivo* mammalian erythrocyte micronucleus test (OECD TG 474) and alkaline comet assay (OECD TG 489), male and female Sprague-Dawley rats (5 per sex/group) were exposed to respirable aerosol of graphene (2.9 to 5.2 µm) via nose only inhalation at measured concentrations of 0.55, 1.00 and 1.92 mg/L (maximum respirable particle dose) for 4 hours/day for 3 days. Bone marrow and lung were collected 3 hours after the last treatment. There were no significant increases in micronuclei in bone marrow or induction of DNA damage in the lung. Study authors concluded that the test substance was not-clastogenic and non-aneugenic (Klimisch 1, reliable without restriction).
- AICIS 2023
 - *In vivo*: In a comet assay (OECD TG not specified), rats were exposed to aerosol of graphene (average lateral dimension: < 2 µm; surface area: 750 m²/g; density: 0.2 g/mL; average thickness of aggregates: 20 – 30 layers) via inhalation at concentrations up to 1.88 mg/m³ for 28 days. The lungs were collected after the treatment. There were no DNA damaged and no increases in inflammatory cytokines or hydrogen peroxide release, both known to mediate oxidative stress and be associated with DNA damage.

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

Graphene (Prophene™ PS100) was assigned a score of Low for reproductive toxicity based on the lack of reproductive toxicity observed in an inhalation reproduction/developmental toxicity screening test in rats performed with graphene of similar particle size. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative and when they are not classified under GHS (CPA 2018b). The confidence in the score is low as it is based on a screening test that may not have examined all relevant endpoints.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025
 - *Inhalation*: In a GLP-compliant reproduction/developmental toxicity screening study conducted according to OECD TG 421, male and female Sprague Dawley rats (10/sex/dose) were exposed by snout only inhalation to graphene nanoform that contains respirable

particles (mass median aerodynamic diameter (MMAD) ≥ 3.5 and $\leq 4.1 \mu\text{m}$ and Geometric standard deviation (GSD) ≥ 2.43 and ≤ 2.55) for 6 h/day, 7 days/week at concentrations of 0, 0.0676, 0.273 or 1.03 mg/L (the maximum achievable concentration). Males were exposed to the test substance during pre-mating phase (14 days), mating phase (2 - 5 days) and post-mating phase (11 - 14 days). Females were exposed to the test substance during pre-mating phase (14 days), mating phase (2 - 5 days), gestation, and up to day 21 of lactation. The parental animals were evaluated for clinical signs of toxicity, body weight, food consumption, estrus cyclicity, sperm parameters, histopathology of the female and male reproductive organs (testes and epididymis and ovaries and uterine content), and reproductive indices (fertility index, gestation index and viability index). Offspring were evaluated for survival, mean litter size, sex ratio, body weight, anogenital distance, nipple retention (male pups), and external and internal abnormalities. There were no treatment related effects on any of the reproductive parameters measured in the treated male or female rats of this study. The study authors identified the reproductive toxicity NOAEC as 1.03 mg/L/6h/day, the highest concentration tested (Klimisch 1, reliable without restriction).

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

Graphene (Prophene™ PS100) was assigned a score of Low for developmental toxicity based on the lack of developmental effects in an inhalation reproduction/developmental toxicity screening test in rats performed with graphene of similar particle size. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data are available and negative, and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on a screening test that may not have examined all relevant endpoints.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025
 - *Inhalation*: In the previously described GLP-compliant reproduction/developmental toxicity screening study conducted according to OECD TG 421, male and female Sprague Dawley rats (10/sex/dose) were exposed by snout only inhalation to graphene nanoform that contains respirable particles (MMAD ≥ 3.5 and $\leq 4.1 \mu\text{m}$ and GSD ≥ 2.43 and ≤ 2.55) for 6 h/day, 7 days/week at concentrations of 0, 0.0676, 0.273 or 1.03 mg/L (the maximum achievable dose). Males were exposed to the test substance during pre-mating phase (14 days), mating phase (2 - 5 days) and post-mating phase (11 - 14 days). Females were exposed to the test substance during pre-mating phase (14 days), mating phase (2 - 5 days) and gestation and up to day 21 of lactation. There were no embryotoxic or teratogenic effects observed with treatment. The study authors identified the developmental toxicity NOAEC as 1.03 mg/L/6h/day, the highest concentration tested (Klimisch 1, reliable without restriction).

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

Graphene (Prophene™ PS100) was assigned a score of Data Gap for endocrine activity based on lack of data for this endpoint.

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

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

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

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

Graphene (Prophene™ PS100) was assigned a score of Low for acute toxicity based on an oral LD₅₀ > 2,000 mg/kg, in mice and an inhalation LC₅₀ > 1.99 mg/m³ (the maximum achievable concentration) in rats. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD₅₀ values are > 2,000 mg/kg, and inhalation LC₅₀ values are > 5 mg/L/4h (dust) and/or when they are not classified per GHS (CPA 2018b). The confidence in the score is low as it is based on measured data from different graphene types with varying particle sizes.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - *Oral:* LD₅₀ (Wistar female rats) > 300 mg/kg for graphene nanoform (lateral dimension: 700-2,000 nm), the maximum attainable dose due to the test item's extremely lightweight nature. No deaths occurred (GLP-compliant, OECD TG 420) (Klimisch 1, reliable without restriction).
 - *Inhalation:* LC₅₀ (Sprague-Dawley rats) > 1.99 mg/L/4-hour aerosol (maximum technically attainable concentration) for graphene nanoform that contains respirable particles (MMAD ≥ 3.5 and ≤ 5.3 μm and GSD ≥ 2.1 and ≤ 2.5) (GLP-compliant, OECD TG 436). No mortalities occurred in a group of ten rats exposed to a mean maximum attainable atmosphere concentration of 1.99 mg/L in air for 4 hours (Klimisch 1, reliable without restriction).
According to GHS criteria, when the inhalation LC₅₀ is greater than the maximum attainable atmosphere concentration, then no classification for acute inhalation toxicity is warranted. Therefore, ToxServices did not classify graphene nanoform per GHS.
- ECHA CHEM, CAS #1034343-98-0, 2025
 - *Oral:* LD₅₀ (ICR mice) > 5,000 mg/kg for graphene (lateral dimension: 700-2,000 nm) (similar to OECD TG 420) (Klimisch 2, reliable with restrictions).

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

Graphene (Prophene™ PS100) was assigned a score of Low for systemic toxicity (single dose) based on the lack of adverse systemic effects and signs of respiratory irritation in acute oral and inhalation toxicity studies with a nanoform graphene with large lateral particle size (lateral dimension: 700-2,000 nm). GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when adequate data are available and negative and they are not GHS classified for systemic toxicity single dose and for aspiration hazard (CPA 2018b). The confidence in the score is low as it is based on measured data from different graphene types with varying particle sizes.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - *Oral:* In a GLP-compliant acute oral toxicity study conducted according to OECD TG 420, five Wistar female rats were administered graphene nanoform in arachis oil at a single dose of 300 mg/kg by gavage. Due to the test item's extremely lightweight nature, the maximum

attainable dose was 300 mg/kg. Animals were observed for 14 days following administration and necropsied for toxicity evaluation. No deaths occurred and no clinical signs of toxicity were seen. Body weight development was not affected. There were no abnormal gross findings at necropsy (Klimisch 1, reliable without restriction).

- *Inhalation:* In a GLP-compliant acute inhalation toxicity study conducted according to OECD TG 436, Sprague-Dawley rats (3/sex/dose) were exposed to graphene nanoform aerosol via nose-only inhalation at concentrations of 0.878 and 1.99 mg/L (analytical), which was the maximum attainable concentration, for four hours. Animals were observed for 14 days. No deaths occurred and no clinical signs of toxicity were seen. Body weight development was not affected. Treatment caused macroscopic changes in the lung (mottled discoloration) in males at 1.99 mg/L and females at ≥ 0.878 mg/L and tracheobronchial lymph node (dark focus) in 1 male at 1.99 mg/L. Authors considered these effects non-adverse as they were due to inert particle load or the experimental procedure (inhalation) and assigned a NOAEC of 1.99 mg/L (the maximum achieved aerosol concentration feasible). (Klimisch 1, reliable without restriction).
- ECHA CHEM, CAS #1034343-98-0, 2025
 - *Oral:* In another acute oral toxicity study similar to OECD TG 420, male and female ICR mice (10/sex) were administered graphene nanoform in arachis oil at a single dose of 5,000 mg/kg by gavage. Animals were observed for 14 days following administration and necropsied for toxicity evaluation. No deaths occurred and no clinical signs of toxicity were seen. Body weight development was not affected. There were no abnormal gross findings at necropsy (Klimisch 2, reliable with restrictions).
- ECHA 2025b
 - Graphene is classified to GHS Category 3 for Specific target organ toxicity – single exposure (Respiratory system) with a hazard statement of H335: May cause respiratory irritation by the majority of aggregated notifiers.
- Based on the weight of evidence, a score of Low was assigned. Although graphene (type unspecified) is classified by the majority of aggregated notifiers to GHS Category 3 for respiratory irritation, the available acute inhalation toxicity study of good quality for graphene of nanoform did not show any signs of respiratory irritation. Similarly, no evidence of systemic toxicity following single oral exposure was reported in acute oral toxicity studies with graphene of nanoform. Thus, ToxServices relied on the measured data and assigned a score of Low for this endpoint.

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

Prophene™ PS100 was assigned a score of Data Gap for systemic toxicity (single dose) based on insufficient data for this endpoint.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any authoritative lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - *Inhalation:* In a subacute inhalation repeated dose toxicity study conducted according to OECD TG 412, male Sprague-Dawley rats (15/dose) were exposed by nose only inhalation to an aerosol of graphene (average lateral dimension: $< 2 \mu\text{m}$; surface area: $750 \text{ m}^2/\text{g}$; density: 0.2 g/mL ; average thickness of aggregates: 20 – 30 layers [size in nm not provided]) at concentrations of 0, 0.12, 0.47 and 1.88 mg/m^3 for 6 hours/day, 5 days/week for 28 days. There were no treatment related effects on body weights, organ weights, bronchoalveolar lavage fluid inflammatory markers, blood biochemical parameters, and lung pathology. The

inhaled graphene was mostly deposited in lung macrophages with some deposition in lung epithelial cells. Translocation of graphene to lung lymph nodes was observed. No adverse lung pathology (no lung epithelial cell proliferation, no inflammatory cell migration to the alveolar space, and no fibroblast proliferation after 90-day recovery period) was reported in exposed animals within any treated groups following recovery. This finding was supported by an absence of any significant increases in inflammatory cells, inflammatory biomarkers or cytokines in the broncho-alveolar fluid or lung tissue lysate in all treatment groups when compared to control animals. Furthermore, no oxidative stress markers (hydrogen peroxide, glutathione and malondialdehyde) were significantly elevated indicating that graphene had no effect on oxidative stress at the concentrations tested. Study authors established a systemic toxicity NOAEC of greater than 1.88 mg/m³ in this study, based on no toxicological effects in rats up to the highest dose tested (equivalent to 1.34 mg/m³/6h/day¹⁰) (Klimisch 2, reliable with restrictions).

- *Due to the 28-day duration of this study, the guidance values were tripled (i.e., 0.2 mg/L/6h/day * 3 = 0.6 mg/L/6h/day) as 28-days is approximately 1/3 the duration of 90-day studies. The NOAEC of 1.34 mg/m³/6h/day (equivalent to 0.00188 mg/L/6h/day* 5 days / 7 days) is below the duration-adjusted GHS guideline value of 0.6 mg/L/6h/day for Category 2 (dust). Therefore, classification is not possible.*
- In a subacute inhalation toxicity study, male Wistar rats (8/dose) were exposed (head-nose) to an aerosol of multi-layer graphene (particle size distribution (SEM) primary structure: ≤ 10,000 nm diameter, flakes; nano pore size: 9 nm, 100 nm, 40,000 nm; purity: approximately 85%) at measured concentrations of 0, 0.54, 3.05 and 10.1 mg/m³ for 6 hours/day for 5 days. There were no treatment related effects on clinical signs of toxicity, body weight, and organ weight. Treatment caused increases of lavage markers indicative of inflammatory processes at exposure concentration of 3.05 and 10 mg/m³. This was associated with microgranulomas that were observed at the high dose. There were no other inflammatory responses and no further alterations of the lung parenchyma. Authors concluded that graphene induced mild lung toxicity at 3.05 mg/m³ and assigned a LOAEC of 3.05 mg/m³. A NOAEC for test material was not reported in this study (Klimisch 2, reliable with restrictions).
- Based on the weight of evidence, a score of Data Gap was assigned. The available two repeated dose inhalation toxicity studies for graphene with various particle sizes indicated that Prophene™ PS100 may have the potential for lung toxicity (e.g. inflammation and microgranulomas) at exposure concentrations of 3.05 mg/m³ or above with even short-term exposures. However, given only short-term inhalation toxicity studies are available and toxicity can be dependent on a number of factors including lateral size of a particle, number of layers and surface chemistry, there remains uncertainty as to the potential lung toxicity of Prophene™ PS100. As the available studies did not test up to the GHS cut-off value for classification, GHS classification for graphene is not possible and thus a score of DG was assigned.

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

Graphene (Prophene™ PS100) was assigned a score of Low for neurotoxicity (single dose) based on the lack of neurotoxic effects in acute oral, and inhalation toxicity studies conducted with graphene nanoform at doses greater than the GHS guidance value for classification or the maximum attainable concentration. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when adequate negative data are available and they are not GHS classified (CPA 2018b). The

¹⁰ Converting exposure period 5days/week to daily = 1.88 mg/m³ x 5 / 7(days) = 1.38 mg/m³/day

confidence in the score is low as it is based on studies with limited neurotoxicity examination for different graphene types with varying particle sizes.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - *Oral*: In the previously described GLP-compliant acute oral toxicity study conducted according to OECD TG 420, five Wistar female rats were administered graphene (nanoform, lateral size: 700 -2,000 nm) in arachis oil at a single dose of 300 mg/kg by gavage. Due to the test item's extremely lightweight nature, the maximum attainable dose was 300 mg/kg. Animals were observed for 14 days following administration and necropsied for toxicity evaluation. No deaths occurred and no clinical signs of neurotoxicity were seen. There were no abnormal gross findings at necropsy (Klimisch 1, reliable without restriction). *Clinical signs of neurotoxicity often evaluated in animal studies include: drowsiness, narcosis, reduced alertness, loss of reflexes, lack of coordination, irritability, fatigue, impaired memory function, deficits in perception and coordination, reaction time, or sleepiness, lethargy, and ataxia. If these effects are not transient in nature, then they shall be considered to support classification for Category 1 or 2 specific target organ toxicity single exposure. As animals in this study did not show any of these signs, ToxServices concluded that the test substance was not neurotoxic in this study.*
 - *Inhalation*: In the previously described GLP-compliant acute inhalation toxicity study conducted according to OECD TG 436, Sprague-Dawley rats (3/sex/dose) were exposed to graphene nanoform aerosol via nose-only inhalation at concentrations of 0.878 and 1.99 mg/L (analytical), which was the maximum attainable concentration, for four hours. No deaths occurred and no clinical signs of neurotoxicity were seen (Klimisch 1, reliable without restriction).
- ECHA CHEM, CAS #1034343-98-0, 2025
 - *Oral*: In the previously described acute oral toxicity study similar to OECD TG 420, male and female ICR mice (10/sex) were administered graphene nanoform in arachis oil at a single dose of 5,000 mg/kg by gavage. Animals were observed for 14 days following administration and necropsied for toxicity evaluation. No deaths occurred and no clinical signs of neurotoxicity were seen. There were no abnormal gross findings at necropsy (Klimisch 2, reliable with restrictions).

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

Graphene (Prophene™ PS100) was assigned a score of Data Gap for neurotoxicity (single dose) based on lack of data for this endpoint.

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

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

Graphene (Prophene™ PS100) was assigned a score of Low for skin sensitization based on negative results in a skin sensitization study for a graphene with large lateral particle size. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative, and when they are not classified per GHS (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for a similar graphene type (non-functionalized).

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - Graphene (nanoform, lateral size:700 -2,000 nm) was not sensitizing in a GLP-compliant Buehler test conducted according to OECD TG 406. Male Hartley guinea pigs (20/dose) were intradermally and epicutaneously (occlusive) induced with 0.25 g of the test substance in 0.9% saline for 24 hours each with a 3-week rest phase. The animals were then challenged with the same dose. No positive reactions were observed in treated animals. The authors concluded that graphene is not sensitizing under the conditions of the assay (Klimisch 1, reliable without restriction).

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

Graphene (Prophene™ PS100) was assigned a score of Low for respiratory sensitization based on the negative skin sensitization data and according to ECHA's recommended strategy on evaluation of respiratory sensitization. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). The confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, no specific data are available for respiratory sensitization, and it is not clear if the ECHA guidance is applicable to inorganic nanomaterials.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As graphene was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by Prophene™ PS100, it is not expected to be a respiratory sensitizer.

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

Graphene (Prophene™ PS100) was assigned a score of Low for skin irritation/corrosivity based on negative results in a dermal irritation study for a graphene with a potentially larger lateral particle size. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and negative, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for similar graphene types (non-functionalized FL).

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - In a GLP-compliant dermal irritation study conducted according to OECD TG 404, 0.5 g graphene (nanoform, lateral size:700 -2,000 nm) moistened with water was applied to the clipped skin of three New Zealand white rabbits for 4 hours under occlusive conditions.

Animals were observed for up to seven days after the exposure period. None of the animals showed erythema or edema at 1, 2, 48, or 72 hours (mean scores is 0). Accordingly, the test substance was determined to be non-irritating under the conditions of the assay (Klimisch 1, reliable without restriction).

- FLG (layer number: 4; lateral dimension distribution: 50-600 nm; lateral dimension: 171 ± 147 nm; carbon content: $94.93 \pm 0.28\%$; impurity: 0.074 mg/L iron) was considered to be non-irritating to skin when tested in a GLP-compliant *in vitro* skin irritation test conducted according to OECD TG 439 using the EpiDerm Human Skin Model after a treatment period of 42 minutes and a 42-hour post-exposure incubation. The relative mean viability of the test item treated tissues was determined to be 101%; which is greater than 50% indicating the substance is not irritating to the skin (Klimisch 2, reliable with restrictions). *Authors of REACH dossier stated that this test is questionable as the OECD TG 439 is not validated for testing on nanomaterials.*

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

Graphene (Prophene™ PS100) was assigned a score of Low for eye irritation/corrosivity based on negative results in an *in vitro* assay conducted according to OECD TG 492 for a graphene with a potentially larger lateral particle size. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when adequate data are available and negative, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on an *in vitro* assay that is acceptable under GHS for classification purpose, for a similar graphene type (non-functionalized).

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - In a GLP-compliant EpiOcular™ *in vitro* eye irritation test conducted according to OECD TG 492, two EpiOcular™ tissue samples were incubated with 50 mg of undiluted graphene (nanoform, lateral size: 700 -2,000 nm) for 6 hours followed by an 18-hour post-incubation period. The mean viability of the test-substance treated tissues was 162.6%; above the threshold of irritants (50%). Accordingly, the test substance did not show an eye irritation potential and was not classified per GHS (Klimisch 1, reliable without restriction). *According to GHS criteria, the OECD TG 492 test can be used only to "Not Classified" for eye irritation when the viability is > 60% (UN 2023).*

Ecotoxicity (Ecotox)

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

Graphene (Prophene™ PS100) was assigned a score of Moderate for acute aquatic toxicity based on measured EC₅₀ values of > 16 mg/L in daphnia (40% lethality at 16 mg/L), and 62 mg/L in algae for two types of graphene (FLG and MLG) with potentially larger lateral particle sizes. GreenScreen® criteria classify chemicals as a Moderate hazard for acute aquatic toxicity when acute aquatic toxicity values are between 10 and 100 mg/L and/or they are classified to GHS Category 3 (CPA 2018b). The confidence in the score is high as it is based on measured data of high quality for the three trophic levels for less toxic forms of graphene.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025

- 96-hour LL_{50} (*Gobiocypris rarus*, fish) > 100 mg/L (OECD TG 203, GLP-compliant). No abnormal behaviour and no mortality were observed (Klimisch 1, reliable without restriction).
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - 48-hour EL_{50} (*Daphnia magna*, invertebrate) > 16 mg/L (immobilization) for FLG with a large particle size (lateral size: 0.5 – 2.0 µm) (unspecified GLP, similar to OECD TG 202). Application of up to nominal 16 mg/L graphene induced 40% daphnid mortality (Klimisch 2, reliable with restrictions). The AICIS stated that the potential for adverse effects increases with smaller particle size, and therefore multi-layer graphene with smaller particle size may cause similar effects to daphnia at similar or lower exposure concentrations. *The evaluated Prophene™ PS100 in this assessment has a smaller lateral size (100 nm - 5 µm), and therefore it may cause similar effects at similar or lower exposure scenarios.*
 - 96-hour EC_{50} (*Chlorella pyrenoidosa*, green algae) for growth rate = 62 mg/L for MLG with a larger lateral size (GLP unspecified, similar to OECD TG 201). Authors stated that the toxicity of the test substance (graphene) to algae is due to nutrient depletion as well as algal cell membrane damage induced by oxidative stress. The AICIS panel also stated that graphene based materials with smaller lateral size are also expected to have similar effects to algae as they interact more readily with the surfaces of algae particles, potentially causing algal growth inhibition at lower concentrations (Klimisch 2, reliable with restrictions). *The evaluated Prophene™ PS100 in this assessment has a smaller lateral size (100 nm - 5 µm), and therefore it may cause similar effects at similar or lower exposure scenarios.*
- Based on the weight of evidence, a score of Moderate was assigned. A slightly larger nano FLG caused 40% mortality at the highest concentration tested, 16 mg/L, in daphnia. Therefore, although the LC_{50} was reported as > 16 mg/L, and the tested concentrations were well above the solubility limit of graphene (< 100 µg/L), there were toxicities observed at above the solubilities. No details were provided on how daphnia mortality occurred or proposed mechanisms of action. This may be related to the form of the test substance (i.e., nano), and hence ToxServices still considered the data in the weight of evidence despite the tested concentrations were above the solubility limit. In the 96-hour algae study with MLG with a larger particle size, toxicities were also observed above the water solubility, with an EC_{50} of 62 mg/L. The study authors reported that there were no shading effects from the test material, as it was poorly dispersible. However, it readily heteroagglomerated with algae, and hence the toxicities observed may result from direct interaction with algae, and from adsorption of macronutrients from the medium, leading to nutrient depletion. ToxServices therefore considered the observed toxicities relevant to this endpoint, despite the reported EC_{50} being above the water solubility.

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): vH

Graphene (Prophene™ PS100) was assigned a score of Very High for chronic aquatic toxicity based on a measured NOEC value of 0.1 mg/L in daphnia for FLG with a potentially larger particle size.

GreenScreen® criteria classify chemicals as a Very High hazard for chronic aquatic toxicity when the chronic aquatic toxicity values are ≤ 0.1 mg/L (CPA 2018b). The confidence in the score is low as it is based on data for graphene with a particle size potentially different from Prophene™ PS100 (FLG with larger particle sizes may accumulate less readily in the organism than graphene with smaller particle size).

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- AICIS 2023

- 96-hour LOEC (*Danio rerio*, fish) for mortality = 0.005 mg/L nominal for pristine graphene (PG; single layer thickness, 170–390 nm lateral) (fish embryo acute toxicity, non-standard). 100% mortality was reported at concentrations of 30 µg/L or higher while developmental effects were observed for embryos exposed to PG at concentrations as low as 5 µg/L. The graphene used in this study has a very small particle size (in terms of thickness and lateral size), and therefore it may more readily accumulate within the chorions of the embryos and cause development damage. As such, this type represents a conservative estimate of fish embryo acute toxicity to graphene.
- 21-day NOEC (*D. magna*, invertebrate) for reproduction = 0.1 mg/L nominal for FLG with larger lateral dimensions (lateral size: 0.5 – 2.0 µm) (OECD TG 211). Exposure to graphene caused reduced size in daphnia offspring and reduced numbers of offspring. The study authors attributed these effects to the accumulation of FLG within the digestive tract of the daphnia, potentially inhibiting nutrient intake (reducing the digestive efficiency and causing malnutrition). The FLG used in this assessment has larger particle size and therefore may accumulate less readily in the organism than graphene with smaller particle size.
 - The particles tested in this study are similar to Prophene™ PS100, in the number of layers (both were FLG), and particle size (0.5 – 2.0 µm vs 0.1 – 5 µm). Therefore, the results reported in this study is relevant to Prophene™ PS100. However, uncertainties exist due to the wide range of lateral particle size for Prophene™ PS100, making it unclear if it would accumulate more or less than the tested graphene in daphnia.
- Based on the above results, the AICIS panel concluded that the assessed graphene (ML-100 and XE) may cause adverse effects in aquatic organisms and impact the development of aquatic organisms when exposure occurs during key developmental stages. It also has potential to cause cell damage to algae.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vH

Graphene (Prophene™ PS100) was assigned a score of Very High for persistence based on graphene not being readily biodegradable when tested according to OECD TG 301 D and based on expert judgment that Prophene™ PS100 is a non-volatile inorganic material, and therefore not expected to partition to the air. In water, soil and sediment, it is expected to be recalcitrant without undergoing biotic or abiotic degradation. GreenScreen® criteria classify chemicals as a Very High hazard for persistence when they are recalcitrant in the environment (CPA 2018b). The confidence in the score is low due to lack of measured half-lives data in the dominant environmental compartments.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025, AICIS 2023
 - Graphene (nanoform, lateral size: 700 -2,000nm) was not readily biodegradable when tested in a GLP-compliant biodegradation test conducted according to OECD TG 301 D (Closed Bottle Test)). Environmental culture (surface water) was exposed to the test substance at concentration of 3.4 mg/L for 28 days. A biodegradation rate of 0% was achieved by the end of the 28-day exposure period (Klimisch 1, reliable without restriction).
- AICIS 2023
 - Graphene consists of nanosheets, nanoplates and nanoparticles of elemental carbon and is chemically stable.

- The AICIS concluded that the two grades of FLG powder (ML-100 and XE) are expected to be persistent in the environment based on data for similar carbon-based materials such as graphite and carbon black. The AICIS stated that biodegradation of graphene requires strong oxidants coupled with acidic conditions and certain naturally occurring enzymes can reportedly biodegrade graphene.

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

Graphene (Prophene™ PS100) was assigned a score of Moderate for bioaccumulation based on studies showing that graphene accumulates in living organisms. However, the presence of organic matter lowers the bioaccumulation potential, as anticipated under environmental conditions. GreenScreen® criteria classify chemicals as a Moderate hazard for bioaccumulation when BCF/BAF values are > 500 to < 1,000 (CPA 2018b). The confidence in the score is low as it is based on expert judgment and due to lack of measured data.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- AICIS 2023
 - The bioaccumulation of graphene nanoparticles (GNP) has been studied in various aquatic organisms such as invertebrates and fish. These studies indicated that GNP accumulates in the living organism and produces potential threats to the developing embryos and fetuses. The size and the interaction of GNP with natural organic matter (NOM) has a significant impact on the accumulation and distribution of GPN with graphene of small lateral dimensions (20–70 nm) of higher concern due to its ability to cross the gut membranes in fish. In addition, the excretion of graphene is generally rapid with feeding and/or in the presence of natural organic matter. *Prophene™ PS100 has lateral dimensions above the 50–70 nm range, therefore its bioaccumulation potential is expected to be low.* The studies are summarized below:
 - In a one exposure bioaccumulation study, adult zebrafish (*Danio rerio*) were exposed to C14-radiolabelled FLG with two different particle sizes (small and large) at various concentrations. The small FLG (S-FLG) has a lateral size of 20–70 nm and 3 layers thickness while the larger FLG (L-FLG) has lateral size of 300–700 nm and 4 layers thickness. Uptake concentrations within the fish were found to be dependent on the exposure concentrations, and peak accumulation was observed to occur after 48 hours of exposure. At a concentration of 250 µg/L, the L-FLG had a higher peak body burden than the S-FLG (48 µg/g dw and 0.29 µg/g dw respectively). The inclusion of natural organic matter in the test solution increased the uptake of both graphene materials (2-fold for L-FLG, 16-fold for S-FLG). The L-FLG was found to accumulate within the digestive tract of the fish, with some minor accumulation on the gills. The S-FLG was found in the guts and the liver of the fish, indicating that the S-FLG was able to pass through the walls of the digestive tract. Depuration of L-FLG was rapid, with 95% excretion after 4 hours in clean water. After 120 hours of depuration, no L-FLG was present within the gut tract of the fish. In contrast, only 30% of S-FLG was able to be excreted after 4 hours of depuration. No further S-FLG was excreted up to 72 hours of depuration. *The L-FLG used in this study has comparable lateral dimensions to Prophene™ PS100, although a portion of Prophene™ PS100's morphologies have a much higher thickness (5-15 layers).*
 - In another exposure bioaccumulation study, uptake by neonatal (< 1 day old) *Daphnia magna* was investigated through exposure to C14-radiolabelled graphene. The graphene used in this study was a mixture of FLG with a lateral dimension of 300 nm, and FLG with a

lateral dimension of 2,000 nm. All FLG was approximately 4 layers thick. Uptake concentrations in daphnia were dependent on the exposure concentrations. The peak body burden of 8 µg/mg dw was observed after 24 hours exposure to a graphene concentration of 250 µg/L. Uptake of the graphene was observed to occur solely within the digestive tract of the daphnia. Depuration of the graphene was affected by the initial exposure concentration and the depuration medium. No depuration of graphene was observed in daphnia exposed to 50 µg/L after 24 hours in clean water, while after 24 hours, 46% and 64% of the graphene was excreted during depuration for the daphnia exposed to 100 and 250 µg/L, respectively. Depuration rates were increased in the presence of humic acid, and when the daphnia was fed algae during depuration. Daphnia that were fed algae during depuration had cleared all graphene from their digestive tract after 10 hours. *Based on this, the AICIS panel concluded that accumulation of the assessed graphene types in invertebrates is not expected to be a concern under environmental conditions, where organic matter is expected to be present, and feeding is expected to occur.*

- Another uptake experiment demonstrated that accumulation of graphene in higher level organisms can occur from consumption of graphene-contaminated biota. While higher body burdens were observed after uptake through diet, when compared to body burdens from exposure to graphene suspensions, levels of accumulation were not indicative of a biomagnification concern for *D. magna* or zebrafish.
- Overall, the AICIS concluded that the assessed graphene (ML-100 and XE) has a potential to accumulate within the digestive tracts and on the gills of aquatic organisms.

Physical Hazards (Physical)

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

Graphene (Prophene™ PS100) was assigned a score of Low for reactivity based on HMIS and NFPA reactivity rating of 0 for another MLG powder with similar physical properties, supported by lack of structural alerts for explosivity. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when available data indicate that the chemical does not warrant GHS classification for any of the reactivity sub-endpoints and the chemical is not present on authoritative or screening list (CPA 2018b). The confidence in the score is low due to lack of measured data.

- Authoritative and Screening Lists
 - *Authoritative*: Not present on any authoritative lists for this endpoint.
 - *Screening*: Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #1034343-98-0, 2025
 - Graphene is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials.
 - Graphene is not considered to have explosive properties as it does not contain any functional groups associated with explosive or self-reactive properties (See Appendix D).
- Energe 2024
 - A safety data sheet for MLG powder (P-PG20) states that it has a reactivity rating of 0 from the NFPA and HMIS, which correspond to “Normally stable, even under fire exposure conditions, and is not reactive with water”¹¹ and “Materials that are normally stable, even under fire conditions, and will not react with water, polymerize, decompose, condense, or self-react. Non-explosives”¹², respectively.

¹¹ <https://www.fm.colostate.edu/files/forms/safety/CH-23.NFPA.ratings.pdf>

¹² <http://www.ilpi.com/msds/ref/hmis.html>

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

Graphene (Prophene™ PS100) was assigned a score of Low for flammability based on the surrogate graphite not being classified as a flammable solid when tested according to EU. A10, supported by the HMIS and NFPA flammability rating of 0 for another MLG powder with similar physical properties. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate data are available and negative, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on measured data of good quality for a strong surrogate.

- Authoritative and Screening Lists
 - *Authoritative:* Not present on any authoritative lists for this endpoint.
 - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #7782-42-5, 2025
 - *Surrogate: Graphite (CAS #7782-42-5):* Graphite was not flammable when tested in a GLP-compliant test conducted according to EU. A10. No ignition was observed during the test (Klimisch 1, reliable without restriction).
- Enerage 2024
 - A safety data sheet for MLG powder (P-PG20) states that it has a flammability rating of 0 from the NFPA and HMIS which corresponds to “Materials that will not burn”, and “materials that are normally stable and will not burn unless heated” , respectively.

Use of New Approach Methodologies (NAMs)¹³ in the Assessment, Including Uncertainty Analyses of Input and Output

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

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

As shown in Table 4, no Type I (input data) uncertainties on using graphene (Prophene™ PS100)’s NAMs dataset (*in vitro* genotoxicity, skin and eye irritation tests) are identified. Graphene (Prophene™ PS100)’s Type II (extrapolation output) uncertainties include the limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions, uncertain applicability of the bacterial reverse mutation assay to testing nanomaterials, the limitation of the *in vitro* skin corrosion test (OECD TG 439) to identify substances classified as mild skin irritant (GHS Category 3), the limitation of the *in vitro* eye irritation test (OECD TG 492) to differentiate between Category 2 and Category 1, or between Category 2A and Category 2, lack of consideration of non-immunological mechanisms of respiratory sensitization, and the uncertainty regarding the applicability of ECHA’s guidance on respiratory sensitization to inorganics and nanomaterials. Some of the type I and type II errors can be alleviated by the use of genotoxicity test batteries in combination with *in vivo* data for skin and eye irritation as there are no validated *in vitro* methods available for the direct identification of Category 2 eye irritants and Category 3 skin irritants, and ECHA’s decision framework to evaluate respiratory sensitization.

Table 4: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses	
Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	<p>Genotoxicity, Skin, and Eye Irritation: No Type I uncertainty is identified on using the <i>in vitro</i> genotoxicity, skin and eye irritation tests as they are considered relevant (appropriate for the evaluation of the corresponding hazards as recommended in the ECHA Guidance), reliable (they have Klimisch scoring of 2 or 1) and adequate (validated methods) (UN 2023).</p> <p>Respiratory Sensitization: No experimental data available, and no validated test methods.</p>
Type II Uncertainty: Extrapolation Output	<p>Genotoxicity: The <i>in vitro</i> chromosome aberration assay (OECD 473) does not measure aneuploidy and it only measures structural</p>

¹³ NAMs refers to any non-animal technology, methodology, approach, or combination thereof that inform chemical hazard and risk assessments. NAMs include *in silico*/computational tools, *in vitro* biological profiling (e.g., cell cultures, 2,3-D organotypic culture systems, genomics/transcriptomics, organs on a chip), and frameworks (i.e., adverse outcome pathways (AOPs), defined approaches (DA), integrated approaches to testing and assessment (IATA).

	<p>chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror <i>in vivo</i> metabolism¹⁴. The mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror <i>in vivo</i> metabolism (i.e. the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).¹⁵ The <i>in vitro</i> bacterial mutagenicity testing is not recommended for nanomaterials as the nanomaterials may not be able to cross the bacterial wall.¹⁶</p> <p>Respiratory sensitization: The applicability domain of ECHA (2017)'s guidance is not clearly defined. The applicability of the guidance to nanomaterials and inorganic chemicals is not known. Additionally, the ECHA guidance (2017) does not evaluate non-immunologic mechanisms for respiratory sensitization.</p> <p>Skin irritation: The OECD TG 439 test is only used to identify irritating substances (GHS Category 2) and non-irritating substances (no category) (UN 2023).</p> <p>Eye irritation: The RhCE test (OECD TG 492) is only used to identify "Not Classified" chemicals. It cannot differentiate between Category 2 and Category 1, or between Category 2A and Category 2B. There is no single <i>in vitro</i> method that can replace an <i>in vivo</i> eye irritation test¹⁷ (UN 2023).</p>	
Endpoint	NAMs Data Available and Evaluated? (Y/N)	Types of NAMs Data (<i>in silico</i> modeling/ <i>in vitro</i> biological profiling/frameworks)
Carcinogenicity	N	
Mutagenicity	Y	<i>In vitro</i> data: <i>in vitro</i> gene mutation assay/ <i>in vitro</i> chromosome aberration assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	N	
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	

¹⁴ <https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352>

¹⁵ <https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE>

¹⁶ https://echa.europa.eu/documents/10162/23047722/appendix_r7a_r7c_hh_v3_peg_en.pdf/cdd3930e-15ab-f7b1-4c6f-2456e0e5530e

¹⁷ https://www.oecd.org/env/ehs/testing/E492_2017.pdf

Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	ECHA's guidance on respiratory sensitization
Skin irritation	Y	<i>In vitro</i> test: OECD TG 439 (reconstructed human epidermis (RHE) test method)
Eye irritation	Y	<i>In vitro</i> test: OECD TG 492 (reconstructed human cornea-like epithelium (RhCE) test method)
Acute aquatic toxicity	N	
Chronic aquatic toxicity	N	
Persistence	N	
Bioaccumulation	N	

References

- Akron Polymer Solutions. 2025. Technical Data Sheet for Prophene™ PS100. Available: <https://www.akronpolymersolutions.com/about-prophene>
- Australian Industrial Chemicals Introduction Scheme (AICIS). 2023. Graphene: AICIS assessment statement. IMAP Group Assessment Report. Dated: 23 March 2013. Available: <https://www.industrialchemicals.gov.au/sites/default/files/2023-10/CA09624%20Assessment%20Statement%20-%20Final.pdf>
- Carbon Waters. 2025. How to differentiate Graphene? Available: <https://www.carbon-waters.com/en/how-to-differentiate-graphene/>
- Clean Production Action (CPA). 2018a. GreenScreen® Assessment Expiration Policy. October 2, 2018.
- Clean Production Action (CPA). 2018b. The GreenScreen® for Safer Chemicals Guidance. Version 1.4 Guidance. Dated January, 2018. Available: https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1.4_2018_01_Final.pdf
- Energe. 2024. Safety Data Sheet for MLG powder (P-PG20) (CAS #1034343-98-0). Revised: 2024. Available: [https://www.graphene.com.tw/upload/pdf/SDS\(P-PG20\)EN-20200915.pdf](https://www.graphene.com.tw/upload/pdf/SDS(P-PG20)EN-20200915.pdf)
- European Chemicals Agency (ECHA). 2017. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint specific guidance. Version 6.0. Dated: July 2017. Available: https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf
- European Chemicals Agency (ECHA). 2025a. Information on Chemicals. Available: <https://echa.europa.eu/et/information-on-chemicals>
- European Chemicals Agency (ECHA). 2025b. Classification and Labeling Inventory (C&L). Available: <https://www.echa.europa.eu/information-on-chemicals/cl-inventory-database>
- European Chemicals Database (ECHA CHEM). 2025. REACH registration dossier for Graphene (CAS #1034343-98-0). Available: <https://chem.echa.europa.eu/>
- European Food Safety Authority (EFSA). 2018. Guidance on Uncertainty Analysis in Scientific Assessments. *EFSA J.* 16(1): e05123. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7009727/>
- Madden, J.C., S.J. Enoch, A. Paini, and M.T.D. Cronin. “A Review of In Silico Tools as Alternatives to Animal Testing: Principles, Resources, and Applications,” *Alt. Lab. Animals* 1-27, (2020). Available: <https://journals.sagepub.com/doi/pdf/10.1177/0261192920965977>
- Organization for Economic Cooperation and Development (OECD). 2020. Overview of Concepts and Available Guidance related to Integrated Approaches to Testing and Assessment (IATA), Series on Testing and Assessment, No. 329, Environment, Health and Safety, Environment Directorate.

Available: <http://www.oecd.org/chemicalsafety/risk-assessment/concepts-and-available-guidance-related-to-integrated-approaches-to-testing-and-assessment.pdf>

Pharos. 2025. Pharos Chemical and Material Library for Graphene (CAS #1034343-98-0). Available: <http://www.pharosproject.net/material/>.

PubChem. 2025. Entry for Graphene (CAS #1034343-98-0). Available:

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

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

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

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

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

United States Environmental Protection Agency (U.S. EPA). 2024. EPA's Safer Choice and Design for the Environment (DfE) Standard. Available: <https://www.epa.gov/saferchoice/standard>

United States Environmental Protection Agency (U.S. EPA). 2025. Safer Chemical Ingredients List (SCIL). Available: <https://www.epa.gov/saferchoice/safer-ingredients>

APPENDIX A: Hazard Classification Acronyms
(in alphabetical order)

- (AA) Acute Aquatic Toxicity**
- (AT) Acute Mammalian Toxicity**
- (B) Bioaccumulation**
- (C) Carcinogenicity**
- (CA) Chronic Aquatic Toxicity**
- (D) Developmental Toxicity**
- (E) Endocrine Activity**
- (F) Flammability**
- (IrE) Eye Irritation/Corrosivity**
- (IrS) Skin Irritation/Corrosivity**
- (M) Mutagenicity and Genotoxicity**
- (N) Neurotoxicity**
- (P) Persistence**
- (R) Reproductive Toxicity**
- (Rx) Reactivity**
- (SnS) Sensitization- Skin**
- (SnR) Sensitization- Respiratory**
- (ST) Systemic/Organ Toxicity**

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Propylene™ PS100 (CAS #1034343-98-0)



 			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
Yes	Graphene	1034343-98-0	DG	L	L	L	DG	L	L	DG	L	DG	L	L	L	L	M	vH	vH	M	L	L


Table 3: Hazard Summary Table							
Benchmark	a	b	c	d	e	f	
1	No	Yes	No	No			
2	STOP						
3	STOP						
4	STOP						

Table 4	
Chemical Name	Preliminary GreenScreen® Benchmark Score
Graphene	1
Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score	


Table 6	
Chemical Name	Final GreenScreen® Benchmark Score
Graphene	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													

APPENDIX C: Pharos Output for Graphene (CAS #1034343-98-0)

 PHAROS

[Comparisons](#) [Common Products](#) [Discussions](#) [Account](#)



1034343-98-0

Graphene

ALSO CALLED (11c)methane, (13c)methane, 74C, a methyl group, Activated carbon NSF, Activated Carbon Powder, Acti...

[View all synonyms \(105\)](#)

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All Hazards View

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		Group I Human					Group II and II* Human								Ecotox			Fate		Physical		Mult	N		
	GREENSCREEN®	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult	PBT	G\
List Hazard Summary	NoGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	pC	-	-	

Hazard Lists

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ENDPOINT	HAZARD LEVEL	GREENSCREEN®	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
T & P and/or B [(Chronic Aquatic Toxicity and Persistence) or (Acute Aquatic Toxicity and Persistence and/or Bioaccumulation)]	pC	NoGS	EU - Manufacturer REACH hazard submissions	H412 - Harmful to aquatic life with long lasting effects (unverified) [Hazardous to the aquatic environment (chronic) - Category 3]	

Restricted Substance Lists (1)

- [Australia - National Industrial Chemicals Notification and Assessments \(NICNAS\): NICNAS](#)


Discussions

No discussions have been posted yet.

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APPENDIX D: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups


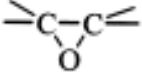
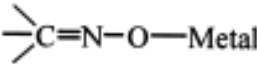
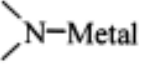
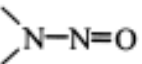
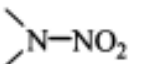
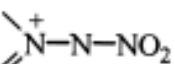
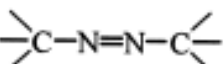
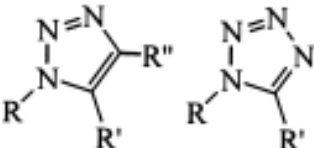
- Not classified if no chemical groups associated with explosivity, e.g.

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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CLP - Substances
31

Explosivity – Full List


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

Chemical group	Chemical Class
-C≡C-	Acetylenic Compounds
-C≡C-Metal	Metal Acetylides
-C≡C-Halogen	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 <i>aci</i> -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) ₂ O, (ArN=N) ₂ S	Bis-Arenediazo Oxides and Sulfides
RN=N-NR'R''	Triazines
	High-nitrogen Compounds: e.g. Triazoles, Tetrazoles

Chemical group	Chemical Class
[1] ROOR', $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \\ \backslash \\ \text{OOR}' \end{array}$ [2]	Peroxy Compounds: [1] Alkyl hydroperoxides (R'=H), Peroxides (R'=organic); [2] Peroxo acids (R'=H), Peroxyesters (R'=organic)
[1] ROOMetal, $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \\ \backslash \\ \text{OO}^+ \text{Metal}^+ \end{array}$ [2]	Metal peroxides, Peroxoacids salts
-N ₃	Azides e.g. PbN ₆ , CH ₃ N 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. perchlorates, bromates, etc
NX ₃ e.g. NCl ₃ , RNCI ₂	N-Halogen Compounds

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

Self-Reactive Substances



Screening procedures

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

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

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CLP - Substances

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APPENDIX E: Change in Benchmark Score

Table 6 provides a summary of changes to the GreenScreen® Benchmark™ for graphene (Prophene™ PS100). This is a new GreenScreen® assessment.

Table 5: Change in GreenScreen® Benchmark™ for Graphene (Prophene™ PS100)			
Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
March 24, 2025	BM-1	v. 1.4	New GreenScreen® assessment.
July 8, 2025	BM-1	v. 1.4	Corrected minor typos.

Licensed GreenScreen® Profilers

Prophene™ PS100 GreenScreen® Evaluation Prepared by:

SIGNATURE
BLOCK

Mouna Zachary, PhD
Senior Toxicologist
ToxServices LLC

Prophene™ PS100 GreenScreen® Evaluation QC'd by:

SIGNATURE
BLOCK

Bingxuan Wang, Ph.D., D.A.B.T.
Senior Toxicologist
ToxServices LLC