

Engineered Nanomaterials

This fact sheet is part of a series of chemical and material fact sheets developed by TURI to help Massachusetts companies, community organizations and residents understand the use of hazardous substances and their effects on human health and the environment. This fact sheet also includes information on safer alternatives and safer use options.

Engineered Nanomaterials: What are They?

Engineered nanomaterials are a diverse set of very small-scale substances. They are commonly defined as engineered objects that have at least one dimension between 1 to 100 nanometers (nm), or roughly 100,000 times smaller than the diameter of a human hair.¹ While some types of nanomaterials occur naturally or are formed incidentally, this fact sheet focuses on nanomaterials that are intentionally designed, engineered and manufactured for use in commercial materials, devices and structures.

There is tremendous variation among engineered nanomaterials. They can vary not only in chemical composition, but also in size, shape, and surface coatings. They can exist as films or sheets, as fibers, horns, rings, tubes, spheres, or irregularly shaped particles. They can be engineered from nearly any chemical substance or mineral.

The physical, chemical and biological characteristics of nano-scale materials can be substantially different from the characteristics of the same substance of a larger size. Material strength, optical properties, conductivity and reactivity of nanomaterials often far exceed that of their larger bulk counterparts. These novel properties have spurred tremendous interest in nanotechnology across many industrial, commercial and medical sectors.

While nanomaterial research and development is still relatively young, these materials are now being used in thousands of industrial and consumer products, including paints and coatings, sensors, photovoltaics, electronics, tires, textiles, sporting goods, and personal care products. They are also being used in medical diagnostic and drug delivery devices, and in environmental remediation.²

Broad categories of nanomaterials

Category	Examples
Metals	Silver, gold, copper
Metal oxides	Titanium dioxide, zinc oxide, iron oxide
Carbon-based	Multi- and single-walled carbon nanotubes, fullerenes
Dendrimers	Hyperbranched polymers, dendrigraft polymers, dendrons
Composites	Nano clays, polymer beads

Human Health and Environmental Concerns

Many of the chemical, biological and physical properties of engineered nanomaterials that make them technologically and commercially desirable are the same properties that make engineered nanomaterials more toxic than the same substance of a larger size. Unbound nanoparticles and nanofibers are of particular concern for human health and the environment because of the potential for exposure. These are engineered nanomaterials that are in loose powder form or suspended in liquids and therefore dispersible, rather than being confined within a matrix or bound to surfaces.

The extremely small size of engineered nanomaterials means they can readily enter the human body through inhalation, ingestion and through the skin. In workplaces, inhalation is a widely recognized route of human exposure. In addition, because nanoparticles have a slow rate of settling, some engineered nanomaterials can remain suspended in air and water for longer periods of times and become more broadly dispersed over wider geographic areas than larger particles of the same size.³

Decades of particle toxicology research have established that particle size influences hazard. As particles become smaller, several key characteristics of the material change compared to their bulk counterpart. At the same exposure dose, compared to micrometer scale particles, nanoscale materials:

- are greater in sheer number;
- have roughly 1,000,000 times greater surface area;
- have enhanced ability to redistribute from their site of deposition and to travel by new pathways, including the lymphatic and nervous systems, to many tissues and organs; and

- have the potential to deliver a higher dose of complex materials attached to their surface.⁴⁻⁶

Substances that are hazardous in bulk form (e.g., cadmium) can generally be expected to be hazardous at the nanoscale. Substances that are not hazardous in bulk form may, however, be hazardous at the nanoscale because of the above nanoscale properties.

Examples of Nanomaterials

The following provides a brief overview of four engineered nanomaterials in which there is strong industrial or commercial interest and/or use, and on which evidence is emerging about effects on human health and the environment: carbon nanotubes, nanosilver, quantum dots, and nano titanium dioxide.

Carbon nanotubes

Carbon nanotubes (CNTs) are hexagonal sheets of carbon (graphite) assembled into tubes – they resemble miniscule rolls of chicken wire. CNTs are divided into two broad categories:

- Single-walled carbon nanotubes (SWCNTs), which may have diameters of approximately 1 nm;
- Multi-walled carbon nanotubes (MWCNTs), which consist of single-walled tubes stacked one inside the other, with diameters ranging from 5 nm to 200 nm.

Carbon nanotubes – properties and uses*	
Types	Single-walled carbon nanotubes (SWCNTs), Multi-walled carbon nanotubes (MWCNTs)
Properties	Excellent tensile strength, thermal and electrical conductivity
Size	SWCNTs: approx. 1 nm (diameter) MWCNTs: 5 to 200 nm (diameter) Lengths vary, from nanometers to millimeters
Uses	Sporting goods equipment, coatings (e.g., anti-static paints), batteries, supercapacitors, sensors, water filtration equipment, photovoltaics, biomedical devices, digital memory devices, among others
*Note: some uses are still in the R&D stage.	

Over the last two decades many different types of CNTs have been produced at the industrial scale. CNTs are now used commercially in a number of applications, including sporting goods, anti-static paints, and sensors. Some applications, such as use as medical devices for drug delivery, are still under investigation.

CNTs can vary dramatically in size, shape and chemical composition, either by design or as a result of contamination during production. They may be straight, bent or curly, rigid or partly flexible. They can exist as single entities or bundled together in ropes or compact tangles that look and act like particles rather than tubes. In addition, they may be functionalized with a wide variety of chemicals on their

surface to enhance desired chemical, biochemical, electrical, or physical properties. They may also contain a variety of contaminants bound to the surface, often as a result of using metal catalysts in manufacturing the nanomaterial. These physical-chemical characteristics determine the inherent functional properties and hazards of a specific carbon nanotube.

Health effects. Over the past decade, toxicological studies have revealed human health impacts primarily due to inhalation exposure hazards:

- **Lung inflammation and fibrosis.** In 2013, the National Institute for Occupational Safety and Health (NIOSH) issued a report based on a comprehensive review of the science and concluded that both SWCNTs and MWCNTs can cause **pulmonary inflammation** and **progressive pulmonary fibrosis** (scarring of the lung).⁷ Physical-chemical characteristics such as metal content and structural defects enhance these toxic effects. Recent studies in manufacturing workers have documented biomarkers of both pulmonary inflammation and fibrosis associated with CNT exposure.⁸
- **Carcinogenicity.** In 2014, the International Agency for Research on Cancer (IARC) classified one type of MWCNTs that have high aspect ratios (long, straight and rigid in their physical characteristics) as a **potential human carcinogen**.⁹ This is based on rodent evidence that this type of MWCNT can cause mesothelioma, a type of cancer that affects the outer lining of the lung or abdomen.
- **Tumor development.** Studies conducted by NIOSH researchers have shown that MWCNTs have the capacity to **promote the development and growth of lung tumors** when test animals are first exposed to a chemical that is known to initiate lung cancer.¹⁰

Adsorption. One important feature of CNTs is their tremendous ability to adsorb other chemicals. This property is being commercialized in the use of CNTs in drinking water filtration devices. However, the presence of CNTs in the environment could increase the bioavailability of other environmental contaminants, such as heavy metals or organic pollutants. Chemical contaminants adsorbed onto CNTs become accessible to organisms for uptake, including soil, terrestrial and aquatic organisms.

Ecotoxicity. CNTs are highly stable and biopersistent – they can reside in an organism for long periods of time. Pure CNTs do not disperse well in water because they are poorly soluble, and also because they often entangle or aggregate/agglomerate. However, the solubility of CNTs can be enhanced if the surface of the CNT is oxidized or if functional groups are added. When CNTs are engineered to

be soluble, studies have identified ecotoxicity concerns. SWCNTs and MWCNTs of various lengths and surface treatments can inhibit the growth of both freshwater and marine algae.¹¹ Studies of aquatic invertebrates document that ingested CNTs (both MWCNTs and SWCNTs) may interfere with food intake and movement at low concentrations,^{12,13} and appear to be more toxic after longer exposures.^{14,15} Studies examining effects on juvenile rainbow trout demonstrate that exposure to SWCNTs dispersed in water caused systemic toxicity, with effects starting at extremely low concentrations (0.1 mg/L). This is considered by the Globally Harmonized System of Classification and Labeling of Chemicals as “extremely toxic to aquatic life.”¹⁶

Quantum dots

Quantum dots (QDs) are nanocrystals. A typical QD is composed of a crystalline semiconductor core encased within another kind of semiconductor material as a shell. The semiconductor core can be comprised of metal complexes, noble metals, and/or magnetic transition metals. QDs containing cores of cadmium (cadmium selenide [CdSe] or cadmium telluride [CdTe]) and shells of zinc sulfide (ZnS) have been used most frequently.¹⁷ QDs can significantly vary in chemical composition, size, charge and surface coatings (i.e., chemical functional groups on the particle surface), depending on the application.

Due to their extremely small size (1–100 nm), QDs have unique electronic and optical properties that create a bright and intense fluorescence as long as the QD is stable. Since their discovery in the 1980s, QDs have been incorporated into medical imaging devices and are currently under investigation as labels for traceable drug delivery and biological probes, as well as drug carriers. They are also being incorporated into solar cells and electronic devices such as LEDs that make use of their optical and electronic properties.

Quantum Dots – properties and uses*	
Types	Can be made from cadmium selenide (CdSe), cadmium telluride (CdTe) and zinc selenide (ZnSe)
Properties	Reactive core influences the material's optical properties
Size	1 to 100 nm
Uses	Medical imaging, photovoltaics, light emitting diodes (LEDs), telecommunication, sensors, drug delivery
*Note: some uses are still in the R&D stage	

Health effects. QDs containing cadmium cores raise concern for human health, as this compound is highly reactive and toxic.

- **Chronic health effects including carcinogenicity.** Bulk level cadmium (Cd) is a known human lung carcinogen and may also cause kidney and prostate cancer.¹⁸ Chronic low-level exposures have also been linked to kidney, bone and lung disease.¹⁹ Despite cancer concerns due to the Cd core in QDs, no carcinogenicity study of Cd-containing QDs has been conducted to date.
- **Health effects related to physiochemical properties.** Research suggests that the toxicity of Cd-containing QDs varies depending on size, chemical surface coatings, and charge, among other characteristics.²⁰ For example, cellular studies indicate that Cd-containing QDs with smaller diameters had greater toxicity compared to larger QDs.²¹ When uncoated, CdSe quantum dots were toxic to liver cells. This toxicity was related to the release of Cd²⁺ ions from the QD core.²² Additional studies have shown Cd ions to be released from QDs with and without a shell layer.²³
- **Respiratory effects.** Studies to date have primarily focused on acute outcomes and how the Cd from QDs distributes throughout the body once exposed. For example, the few respiratory toxicology studies conducted to date have observed dose-dependent lung injury and inflammation with CdSe QDs that were functionalized with carboxyl or amine groups. Researchers suggest that the toxicity findings appear dependent on the dissolution of the QD structure and the subsequent bioavailability of free Cd.²⁴ After pulmonary exposure, the kidneys appear to be the main organ from which Cd from the QDs is distributed to other organs. This is also true of bulk Cd.^{24,25}

Ecotoxicity. Current evidence indicates that cadmium-containing QDs can accumulate and exert toxic effects on micro-organisms, invertebrates and fish species in both freshwater and seawater.²⁶ UV radiation appears to increase the toxicity of QDs.²⁶ Ecotoxicity in organisms at the different trophic levels is dependent on physical-chemical properties, among other factors such as environmental conditions. Examples of toxicity effects include reduction in algal photosynthetic activity and growth inhibition,^{27,28} DNA damage in invertebrates,^{29,30} and decreased cell viability and DNA damage in various fish species.^{30,31}

Nano titanium dioxide

Nano titanium dioxide (TiO₂) is derived from three crystalline forms of titanium dioxide: rutile, anatase and brookite. For decades, TiO₂ at the nanoscale has been used as a whitening agent in paints and pigments and as an anti-caking agent. In addition to these industrial uses, nano TiO₂ is widely used in cosmetics and sunscreens and in some food products such as chewing gum.

TiO₂ is generally thought to be a low toxicity substance. However, its toxicity changes at the nanoscale. Studies demonstrate that nano TiO₂ particles (about 20-30 nm) are considerably more toxic than micrometer-sized TiO₂ (>100nm).^{32,33}

Nano titanium dioxide	
Types	Crystalline nano forms: rutile, anatase and brookite
Properties	Whitening agent, anti-caking agent
Size	10 to 200 nm
Uses	Paints, coatings, printer ink, plastics, household products, cosmetics, sunscreens, food products

Health effects. NIOSH issued a report based on a comprehensive review of health effect studies. The report reviewed impacts associated with different sizes of TiO₂, including the nanoscale. For nano TiO₂, the report documented toxicological evidence of:³⁴

- **Pulmonary inflammation.** Nano TiO₂ can both cause pulmonary inflammation and exacerbate pre-existing symptoms.
- **Genotoxicity.** Under certain conditions nano TiO₂ can damage DNA (e.g., nano TiO₂ particles exposed to UV light; specific TiO₂ particle types).
- **Carcinogenicity.** NIOSH determined that occupational exposure (by inhalation) to nano TiO₂ particles should be considered a potential occupational carcinogen.
- **Organ effects.** Nano TiO₂ accumulates particularly in the liver even at low exposure levels. Toxicological effects have been observed on the liver, but at generally very high doses.³⁵

Although studies suggest that intact skin does appear to block nano TiO₂ from entering the body, the European Union’s Scientific Committee on Consumer Safety recommended that cosmetics and sunscreens containing nano TiO₂ not contain particles with high photocatalytic activity, which enhances toxicity.³⁶

Ecotoxicity. Because of widespread industrial and consumer use, there is concern about releases of nano TiO₂ into the environment. Studies have observed effects on some aquatic fish species,³⁷⁻³⁹ yet the greatest impact may be the ability of TiO₂ to adsorb and enhance the bioavailability of other toxic contaminants in the aquatic environment, including lead, arsenic and cadmium.⁴⁰⁻⁴² As with other nanomaterials, the aquatic toxicity of TiO₂ is dependent on factors such as solubility, pH of the aquatic system, and state of agglomeration.

Nanosilver

Unlike most engineered nanomaterials, nanosilver is not a recent innovation. Colloidal silver is a form of silver that is based on extremely small particles and has been used for medical applications for over 100 years.

In recent years, however, the use of nanosilver has increased dramatically. Silver in all forms has antimicrobial properties. However, the nonspecific antimicrobial function of nanosilver has resulted in its broad use in commercial and consumer products, including food preparation equipment, personal care products, textiles, paints and pigments, and wound dressings, among others.⁴³

Nanosilver – properties and uses	
Types	Colloidal silver, spun silver, nanosilver powder and polymeric silver
Properties	High surface reactivity, strong antimicrobial properties
Size	10 to 200 nm
Uses	Medical devices and wound dressings, paints and pigments, water purification, insecticides, and antimicrobial uses in a wide variety of consumer products (e.g., children’s toys, textiles and shoes, cosmetics and personal care products, food preparation tools and appliances)

Ecotoxicity. Studies demonstrate that nanosilver, like bulk silver, is **toxic to aquatic species**, including various invertebrate, algae and fish species.⁴⁴⁻⁴⁷ One analysis evaluated the existing ecotoxicity data, using the Globally Harmonized System of Classification and Labeling of Chemicals, and classified nanosilver as “acutely very toxic” and “potentially chronically very toxic.”⁴⁸ These findings are concerning because nanosilver is often released from the material on which it is used (e.g., textiles, food preparation surfaces) and can enter municipal wastewater treatment systems as well as contaminating rivers, lakes and ocean water bodies.⁴⁹

Concerns for wastewater treatment and agriculture.

Particular concerns have been raised about the effect of nanosilver on wastewater treatment systems that depend on microbial activity, and the effect of nanosilver in wastewater sludge that is often applied to agricultural fields.⁵⁰ Studies are not consistent as to whether nanosilver is more toxic than bulk silver. The study results appear to be influenced by factors including the dose metric (measuring mass versus particle number), solubility, and the ability of nanosilver particles to agglomerate in the environmental media. As with all nanomaterials, the types of surface coatings can alter the environmental fate of nanosilver and its toxicity.

Health effects. A draft NIOSH report, based on a comprehensive review of available published studies, concludes that there are risks of lung and liver effects, including lung inflammation, associated with exposure to

silver nanoparticles in the range of 15-20 nm.⁵¹ These findings are based on oral and inhalation toxicological studies (90 day studies in rats) that observed:⁵²⁻⁵⁶

- **Lung effects.** Exposure was associated with compromised lung function and lung inflammation.
- **Organ effects.** Once deposited in the lung, nanosilver can be transported in the blood to cause cellular changes in the kidneys and liver. Signs of liver necrosis have been observed.
- **Deposition in spleen, olfactory bulb and brain.** Beyond the lungs, liver and kidneys, significant increases in the amount of silver after exposure have been observed in the spleen, olfactory bulb, and brain.

Additional health concerns. *In vitro* cellular studies summarized in the NIOSH report show that once nanosilver is present in organs and tissues, it can cause DNA damage, genotoxicity, oxidative stress and cell death. Scientists have also noted that **antimicrobial resistance** is a growing concern.^{57,58}

Safer Alternatives

There remains significant uncertainty regarding the health and environmental effects of engineered nanomaterials.

Commercialization of products and processes containing nanomaterials should not proceed until their hazards are well understood.

When making decisions about product design, it is important to consider whether the function proposed for a nanoparticle is necessary or if it can instead be achieved using a bulk material. For numerous functions in a given application, such as material strength or optical properties, existing bulk materials may satisfactorily achieve the desired function and should be used instead of nanomaterials, given significant data gaps regarding the health and safety of nanomaterials.

Considerations for the Safer Development and Safer Use of Engineered Nanomaterials

There is growing interest in “green” nanotechnology – reducing hazard through appropriate design and applications of engineered nanomaterials. Green nanotechnology straddles two disciplines: green chemistry and green engineering. Both of these disciplines consider hazard across the life cycle as an inherent property of chemicals and materials. Hazard is seen as a design attribute – more specifically a design flaw – and considered part of the feasibility equation, on equal footing with technical and economic feasibility considerations.

Researchers at TURI have started such a blueprint for design rules for safer nanotechnology. The design rules include five

principles, which together follow the acronym SAFER, as shown in the table below.⁵⁹ These principles focus on aspects such as modifying physical-chemical characteristics of the material to diminish the hazard, considering alternative materials, and enclosing the material within another, less hazardous, material.

Other researchers have proposed other more specific design rules, which include avoiding chemical compositions of engineered nanomaterials that contain known toxic elements such as cadmium, and avoiding nanomaterials with dimensions that are known to possess hazardous properties (such as CNTs that resemble asbestos fibers).⁶⁰

Design Principles for SAFER Nanotechnology ⁵⁹	
1. Size, surface and structure:	Diminish or eliminate the hazard by changing the size, surface, or structure of the nanoparticle while preserving the functionality of the nanomaterial for the specific application
2. Alternative materials:	Identify either nano or bulk safer alternatives that can be used to replace a hazardous nanoparticle
3. Functionalization:	Add additional molecules (or atoms) to the nanomaterial to diminish or eliminate the hazard while preserving desired properties for a specific application
4. Encapsulation:	Enclose a nanoparticle within another less hazardous material
5. Reduce the quantity:	In situations where the above design principles cannot be used to reduce or eliminate the hazard of a nanomaterial, and continued use is necessary, investigate opportunities to use smaller quantities while still maintaining product functionality

In addition to **eliminating** nanomaterials or **reducing** their toxicity whenever possible, **safer workplace practices** are essential. Facilities using engineered nanomaterials, including research labs as well as industrial and commercial enterprises, must follow strict procedures to ensure the protection of workers, consumers, communities and the environment. At a minimum, entities using engineered nanomaterials or products with nanomaterials should have in place and implement a risk management program that includes:^{61,62}

- Evaluating available hazard information for the nanomaterials used on site (e.g., physical-chemical properties, toxicology, health effects data);
- Assessing employees’ job tasks to determine the potential for exposure;
- Educating and training all employees regarding the proper handling of engineered nanomaterials;
- Prohibiting cleaning with dry methods, such as sweeping or blowing air;
- Containing all potential release points of engineered nanomaterials by installing and evaluating engineering controls (e.g., exhaust ventilation) and environmental

control technologies to prevent any releases to the environment;

- Selecting proper personal protective equipment; and
- Systematically and continuously evaluating exposures to ensure that occupational and environmental control measures are working properly.

Sophisticated risk management programs such as this can only be developed and implemented by health and safety professionals trained in the unique challenges of engineered nanomaterials. Small start-up companies and others without such capabilities on staff should seek outside expertise, such as consultants or state health departments.

Regulatory Context

There are currently no Massachusetts regulations specifically governing the use or release of nanomaterials. Other states, however, have pursued regulations focused primarily on understanding use characteristics, analytical testing methods and environmental health and safety data if known. For example, in 2010-11, California invoked its authority to request information from companies manufacturing or using specific nanomaterials of concern in California, including carbon nanotubes, quantum dots, nanosilver and nano titanium dioxide, among others.⁶³ In 2006, Berkeley, California, was the first city to issue an ordinance requiring facilities that manufacture or use nanomaterials to report and disclose to city officials the current toxicology and occupational and environmental risk management controls that are in place to mitigate impacts.⁶⁴

At the federal level, nanomaterials are primarily regulated by the Environmental Protection Agency (EPA) under the Toxics Substances Control Act (TSCA). Chemical substances under TSCA are regulated on the basis of their Chemical Abstract Service (CAS) identification number – a system that differentiates based on molecular structure, not size. For the majority of nanomaterials, including nanosilver and nano TiO₂, TSCA does not differentiate between the nano form and the bulk form. These nanomaterials are regulated as “existing chemicals” under TSCA. However, some nanomaterials, including QDs and CNTs, are subject to “new chemical” provisions under TSCA. For nanomaterials considered a “new chemical,” manufacturers must submit a PreManufacturing Notice (PMN). In many cases, EPA has subsequently issued Significant New Use Rules (SNURs) for these materials. As of 2017, companies using or manufacturing nanomaterials that have not been subject to PMNs or SNURs will be subject to a one-time reporting and recordkeeping rule (see table).⁶⁵

Other EPA statutes also apply to nanomaterials. If a pesticidal claim is made about a nanomaterial product, it is subject to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

Although the EPA National Ambient Air Quality Standards (NAAQS) regulate particulate matter in air that is smaller than 2.5 µm (PM_{2.5}), these regulations currently do not specifically address nano-sized particles as distinct from particles in the micrometer size range.⁶⁴ If engineered nanomaterials enter drinking water, they may be regulated under the Safe Drinking Water Act although no maximum contaminant level goals (MCLGs) and maximum contaminant levels (MCLs) have been established for nanomaterials based on their nano-size properties.

The Occupational Safety and Health Administration (OSHA) has issued no permissible exposure limits (PELs) for engineered nanomaterials. NIOSH has published recommended exposure limits (RELs) for CNTs⁷ and nano TiO₂,³⁴ as shown in the table below.

Regulatory Considerations	
Occupational Exposure Limits*	<ul style="list-style-type: none"> • CNTs: NIOSH REL⁷: 1 µg/m³, as elemental carbon • Nano titanium dioxide: NIOSH REL³⁴: 0.3 mg/m³ • Nanosilver: NIOSH’s draft (2015) report stated that there is not enough available data to develop a REL for nanosilver and recommends that worker exposures to nanosilver not exceed the current REL for silver of 10µg/m³.⁵¹
EPA	<p>Federal Insecticide, Fungicide and Rodenticide Act</p> <ul style="list-style-type: none"> • Companies making pesticidal claims about a nanomaterial product must comply with FIFRA and register the pesticide with EPA. Conditional registrations have been issued for certain nanosilver anti-microbial products. However, in June 2017, the U.S. Court of Appeals for the Ninth Circuit revoked the conditional approval for the product “Nanosilva.”⁶⁶
	<p>Toxics Substances Control Act</p> <ul style="list-style-type: none"> • EPA requires manufacturers and importers of nanomaterials that are considered “new chemicals” to submit a premanufacture notice (PMN) to EPA at least 90 days in advance of a new chemical’s commercialization. EPA approval is based on consent orders between EPA and the particular firm, which outline the terms of use, including environmental and health protections and toxicity testing requirements. • Significant New Use Rules (SNURs). SNURs have been issued for dozens of nanomaterials that were previously the focus of PMNs. • Companies that manufacture (including import) or process certain chemical substances already in commerce as nanoscale materials must comply with a one-time reporting and recordkeeping rule and notify the agency of specific information, including specific chemical identity; production volume; methods of manufacture; processing, use, exposure and release information; and available health and safety data. Some exceptions apply. The rule goes into effect on August 14, 2017 and reporting is required by August 14, 2018.
*REL: Recommended Exposure Limit, based on an 8-hour time weighted average.	

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