TECHNICAL INFORMATION 1415

AEROSIL® and AEROPERL® Pharma Colloidal Silicon Dioxide Products

EVONIK
POWER TO CREATE

Table of Contents

1. AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide – the optimal glidant and beyond

AEROSIL® colloidal silicon dioxide[1] has been used as a pharmaceutical excipient[2,3] since the early days of direct compression tableting[4]. AEROSIL® 200 Pharma is the traditional glidant, helping to obtain the optimal powder flow required by today's high speed tablet presses. Since the time that AEROSIL® 200 Pharma was first used as a glidant, challenges in formulating solid dosage forms have become more complex. Tablet powders of different average particle size, composition and moisture sensitivity are common in the industry – requiring specialized products to be able to compete in an increasingly cost sensitive health care environment. To support the industry in coping with these challenges Evonik has introduced more AEROSIL® and AEROPERL® Pharma colloidal silicon dioxides to the market not only to provide optimal glidants for almost any tableting process, but also to help the pharmaceutical industry with other formulation challenges such as:

- implement more efficient or economical granulation processes
- incorporating liquids or solutions into solid dosage forms (e.g. liquid or dissolved actives)
- controlling the rheology and helping to stabilize semisolid dosage forms against thermal degradation
- improving the dissolution of poorly soluble active pharmaceutical ingredients.

[1] This brochure uses the term "colloidal silicon dioxide" in the sense of the USP/NF monograph for silica products produced by flame hydrolysis. Products of this kind are also known as fumed silica in other industries. The products are not to be mistaken as "colloidal silica" or "silica sol" which stands for dispersions of spherical silica particles in a fluid (typically water). For an overview of the different forms of silica please refer to the chapter "Silica" in Ullmann's Encyclopedia of Industrial Chemistry, Wiley and Sons.

[2] Galenic considerations on AEROSIL® (in German) von Czetsch-Lindenwald, H. Die Pharmazie 12 (12) (1957) 589 - 592.

[3] Galenic considerations on AEROSIL® II (in German) von Czetsch-Leisenwald, H, Die Pharmazie 12 (12) (1957) 810 - 811.

[4] On direct compression of tablets (in German) Tawashi, R. Pharmazeutische Industrie 26 (1964) 682 - 685.

Table 1 gives an overview of all AEROSIL® and AEROPERL® Pharma products with their characteristics, physico-chemical properties and their compliance to the different pharmacopoeia monographs.

Table 1
Physico-chemical properties and pharmacopoeia compliance of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide

		AEROSIL® 200 Pharma	AEROSIL® 200 VV Pharma	AEROSIL® 300 Pharma	AEROSIL® R 972 Pharma	AEROPERL® 300 Pharma
Characteristics	Type	Powder	Densified powder	Powder	Powder	Granulate
	Behavior in water	Hydrophilic	Hydrophilic	Hydrophilic	Hydrophobic	Hydrophilic
Typical physico-chemical properties	Specific surface area (BET, in m^2/g)	175–225	175–225	270–330	90–130	260–320
	Tapped density (in g/L)	Appr. 50	Appr. 120	Appr. 50	Appr. 50	Appr. 270
	pH	3.5–5.5	3.5–5.5	3.5–5.5	---	3.5–5.5
Pharmacopoeia compliance	Europe (Ph. Eur.)	Silica, colloidal anhydrous	Silica, colloidal anhydrous	Silica, colloidal anhydrous	Silica, hydrophobic colloidal	Silica, colloidal anhydrous
	USP/NF	Colloidal silicon dioxide	Colloidal Silicon Dioxide	Colloidal Silicon Dioxide	Hydrophobic Colloidal Silica	Colloidal Silicon Dioxide
	JP	Light anhydrous silicic acid	---**	---	---***	---**
	China (ChP)	Colloidal silicon dioxide* (Jiaotai Eryanghuagui)	---	---	---	---
	India (IP)	Colloidal silicon dioxide	---	---	---	---

* Chinese Pharmacopoeia values are not included on the certificates of analysis. However, AEROSIL® 200 Pharma complies with the quality requirements set forth in monograph "colloidal silicon dioxide" (Jiaotai Eryanghuagui)
** The material fulfills all tests in the JP except the volume test which test the bulk density.
*** There is no monograph for a hydrophobic silica in JP.

AEROSIL® 200 Pharma is and remains the traditional and most popular glidant for solid dosage forms which has set the standard in the industry. The powder has a high specific surface area, is hydrophilic in nature and features almost universal pharmacopoeia compliance.

In cases where storage space and handling of a low density powder is a challenge we recommend AEROSIL® 200 VV Pharma. The product overall has the same physico-chemical parameters as AEROSIL® 200 Pharma but due to a special production step (described in chapter 2.3) double of the density. Storage of the same amount of AEROSIL® 200 VV Pharma compared to AEROSIL® 200 Pharma only requires about half of the floor space. The higher density of the material also results in more favorable powder handling properties, including reduced dust generation.

Compared to the standard glidant, AEROSIL® 300 Pharma features a higher specific surface area. This special property leads to an increased absorption ability, making the material the preferred solution for anti-caking applications. AEROSIL® 300 Pharma is a very efficient thickener for oils of low polarity.

AEROSIL® R 972 Pharma is different from all of the so far mentioned products as it is surface modified, and thereby rendered hydrophobic. The hydrophobic nature of the material is achieved by the irreversible anchoring of organic dimethylsilyl groups on the surface. The surface modification makes the material better compatible with oils in semi-solid dosage forms and can help to protect moisture sensitive or hygroscopic actives in tablets and capsules.

Unlike the powdered AEROSIL® Pharma products AEROPERL® 300 Pharma is a granulated version having a high density in the range of 270 g/L. AEROPERL® 300 Pharma features mesoporous granular particles with a median particle size between 20 and 60 µm. The granulate due to its porosity is an excellent inert pharmaceutical absorbant.

Table 2 introduces some typical uses of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide in pharmaceutical formulations. The wide field of applications for AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide, however, is not covered in this brochure but is the topic of more specialized Technical Information brochures that are available from the www.aerosil.com webpage.

Table 2
AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide applications

Dosage forms	Applications	Products
Solid dosage forms • tablets • capsules	Glidants • Assisting powder flow • Preventing powder caking • Optimizing tablet weight uniformity • Improving mechanical tablet stability	AEROSIL® 200 Pharma AEROSIL® 200 VV Pharma AEROSIL® 300 Pharma AEROSIL® R 972 Pharma
	Carrier • Cost optimization of granulations • Incorporation of liquids and solutions • Improving dissolution of poorly soluble active pharmaceutical ingredients	AEROPERL® 300 Pharma
Semisolid dosage forms • Gels, ointments, salves • Transdermal therapy systems • Suppositories	Rheology control • Viscosity adjustment • Stabilization of dispersions • Heat stabilization of suppositories	AEROSIL® 200 Pharma AEROSIL® 300 Pharma AEROSIL® R 972 Pharma
	Surface effects • Stabilization of emulsions	AEROSIL® R 972 Pharma

2. Manufacture of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide

All AEROSIL® and AEROPERL® Pharma products are based on a continuous gas phase, flame hydrolysis process. Starting from the material produced in this process AEROSIL® 200 VV Pharma (densification), AEROSIL® R 972 Pharma (hydrophobic post-treatment) and AEROPERL® 300 Pharma (granulation) are generated in consecutive steps to create their specific product properties.

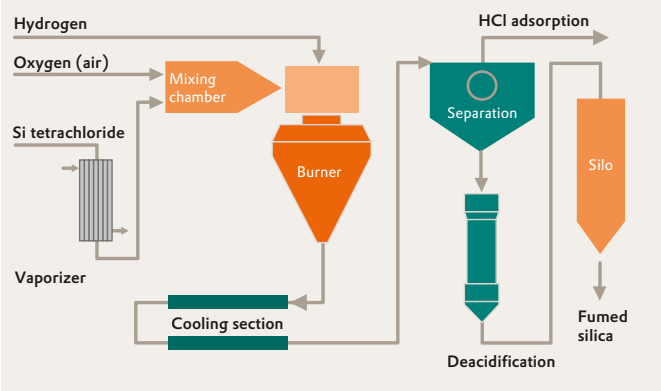
2.1 FLAME HYDROLYSIS

AEROSIL® Pharma colloidal silicon dioxide is manufactured by the hydrolysis of silicon tetrachloride in a hydrogen oxygen flame according to the following overall chemical reaction:

$$SiCl_4 + 2\ H_2 + O_2 \rightarrow SiO_2 + 4\ HCl$$

During the manufacture of AEROSIL® Pharma colloidal silicon dioxide, vaporized silicon tetrachloride is hydrolyzed with very hot steam formed by a hydrogen oxygen flame. The reaction results in the formation of AEROSIL® Pharma fumed silica particles and hydrogen chloride gas as a by-product. AEROSIL® Pharma colloidal silicon dioxide is de-acidified and separated from the gaseous by-products. The process which is described in more detail in figure 3, uses exceptionally pure raw materials of exclusively inorganic nature. Neither metal catalysts, organic solvents nor materials of natural or biogenic origin are used, producing an exceptionally pure amorphous powder with a silicon dioxide content of more than 99.8 % by weight (based on the dried substance). The elemental impurity content of the material is below the threshold values given in table A2.2 for Option 1 of the ICH Q3D Guideline[5] and the pharmacopoeia requirements based on it. Due to the high chemical purity AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide features good compatibility even with active pharmaceutical ingredients having a high sensitivity to heavy metals. Figure 4 shows the particle structure of AEROSIL® Pharma colloidal silicon dioxide. The material features aggregates as the smallest units. These aggregates form agglomerates that are held together by van der Waals and hydrogen bonds. Due to the comparatively weak forces that hold together the agglomerates de-agglomeration occurs when AEROSIL® Pharma colloidal silicon dioxide is mixed with other powders or dispersed in liquid matrices. This de-agglomeration will ultimately lead to free aggregates as the smallest units of the material being present in these mixtures. The so-called primary particles that

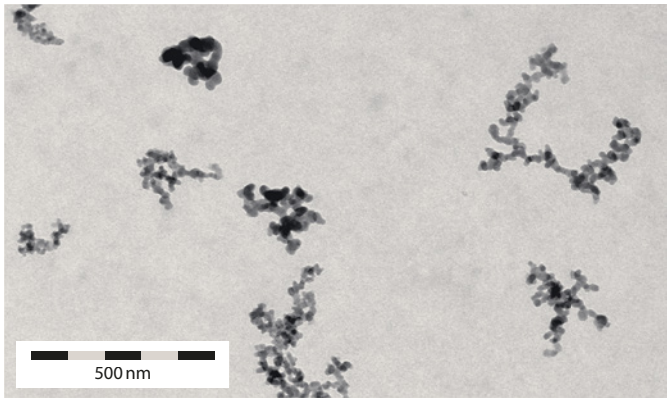
FIGURE 3: FLAME HYDROLYSIS PROCESS



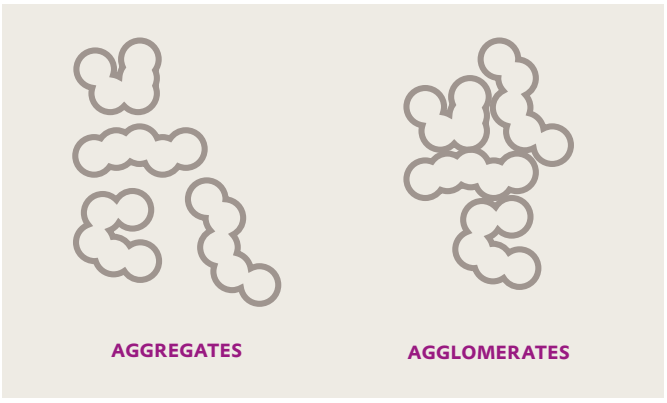
[5] Option 1 offers the simplest way to show compliance with the ICH Q3D guideline. The option can be used for pharmaceutical preparations with daily dosage of 10 g or less. Table A2.2 list the limits of metals in each ingredient present in the preparation.

are visible in electron microscopy pictures of AEROSIL® Pharma colloidal silicon dioxide do not exist separated from each other but are bound together by covalent bonds to form aggregates. However, the particle size given in the European Pharmacopoeia monograph "Silica, Colloidal Anhydrous" refers to the approximate size of these primary particles. Siloxane and silanol groups cover the surface of hydrophilic AEROSIL® Pharma colloidal silicon dioxide. The silanol groups are responsible for the high affinity of the material for water and polar compounds. Hydrophilic AEROSIL® Pharma colloidal silicon dioxide is able to adsorb considerable quantities of water without any change in its state of aggregation.

FIGURE 4: STRUCTURE OF AEROSIL® PHARMA COLLOIDAL SILICON DIOXIDE



Transmission electron microscopy image of AEROSIL® 200 Pharma obtained after dispersing the material by ultrasound in isopropanol/water.



A graphic model of AEROSIL® Pharma colloidal silicon dioxide aggregates.

2.2 HYDROPHOBIC POST-TREATMENT

To produce hydrophobic AEROSIL® R 972 Pharma, hydrophilic colloidal silicon dioxide is reacted with dimethyldichloro silane in a consecutive reaction step that follows immediately after the generation of silica particles in flame hydrolysis (Figure 5). This step is also conducted at high temperature. As a result, dimethylsilyl groups are irreversibly covalently bound to the surface of the colloidal silicon dioxide particles by very stable siloxane bonds, resulting in a product that neither mixes with water nor absorbs water from the atmosphere (Figure 6). The hydrophobic treatment also reduces the silanol group density at the surface of the silica.

FIGURE 5: REACTIONS OF THE SURFACE MODIFICATION TO PRODUCE AEROSIL® R 972 PHARMA

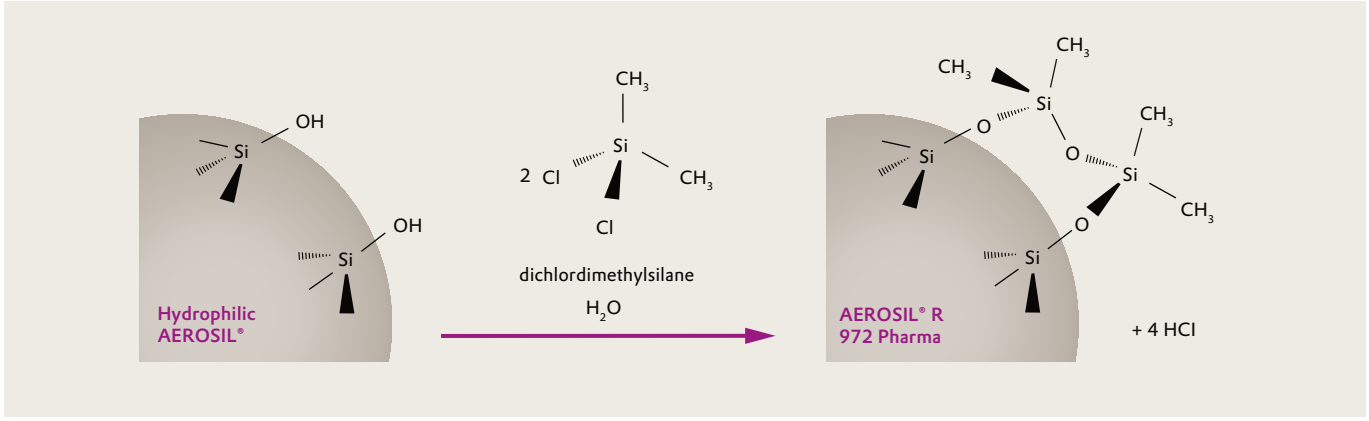
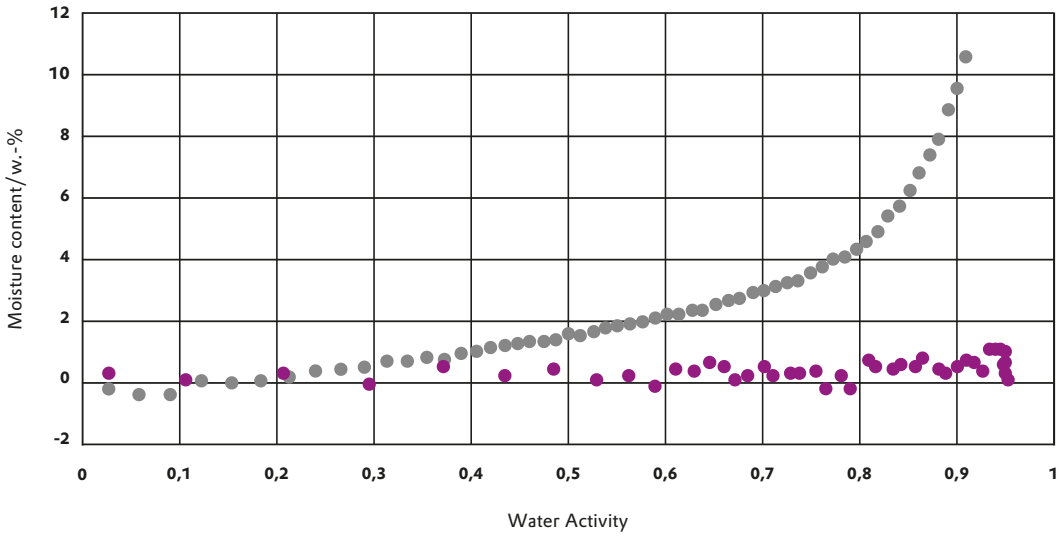


FIGURE 6: WATER ABSORPTION ISOTHERM OF AEROSIL® 200 PHARMA AND AEROSIL® R 972 PHARMA

Experimental: samples were contacted with gas streams of water activity aw = 0,03 to aw 0,95 a flow rate of 80 ml/min at 25 °C.



2.3 DENSIFICATION

AEROSIL® Pharma agglomerates are irregular in size and shape and do not pack well. The considerable amount of void space between the agglomerates is responsible for the low density of traditional colloidal silicon dioxide.

AEROSIL® 200 VV Pharma is a densified grade. Using a purely mechanical densification technology, air is removed from between the agglomerates. The result is larger, more-stable, secondary agglomerates that produce considerably less fine dust (particles < 10 - 20 µm in size) than traditional non-densified colloidal silicon dioxide. Due to the purely physical nature of the densification the typical physico-chemical properties such as specific surface area are not affected. The only difference of the two products is the tapped density, which for AEROSIL® 200 VV Pharma is about 120 g/L compared to 50 g/L for the non-densified AEROSIL® 200 Pharma.

Literature

Investigation of compacted hydrophilic and hydrophobic colloidal silicon dioxides as glidants for pharmaceutical excipients. Jonat, S., Hasenzahl, S., Drechsler, M., Albers, P., Wagner, K. W., Schmidt, P. C. Powder Technology, 141 (1-2) (2004) 31-43.

Investigation of the glidant properties of compacted colloidal silicon dioxide by angle of repose and X-ray photoelectron spectroscopy, Jonat, S., Albers, P., Gray, A., Schmidt, P.C., European Journal of Pharmaceutics and Biopharmaceutics 63 (2006) 356–359.

2.4 GRANULATION

By processing, AEROSIL® Pharma powder can be transformed into round shaped granules with high porosity (Figure 7). The granulate AEROPERL® 300 Pharma has an average particle size between 20 and 60 µm and is highly porous, with pores predominantly in the mesoporous range between 2 and 50 nm (Figure 8). The material has a very high tapped density of approximately 270 g/L unmatched by any AEROSIL® Pharma product. The round particle shape imparts exceptional powder flow to the granules.

Due to its unique physico-chemical properties AEROPERL® 300 Pharma is a highly effective absorbent and carrier for a multitude of different applications.

FIGURE 7: SCANNING ELECTRON MICROSCOPY (SEM) IMAGE OF AEROPERL® 300 PHARMA

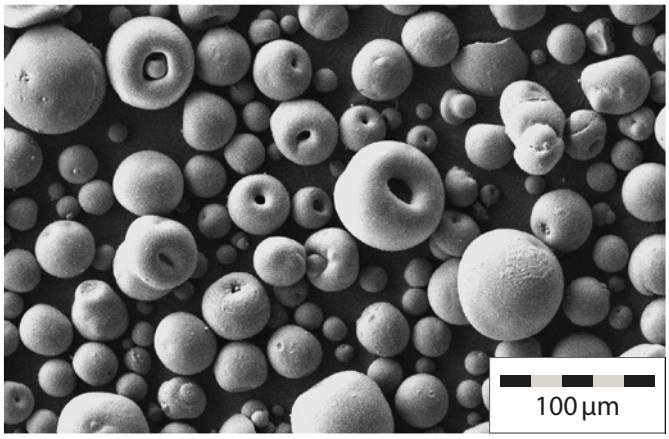
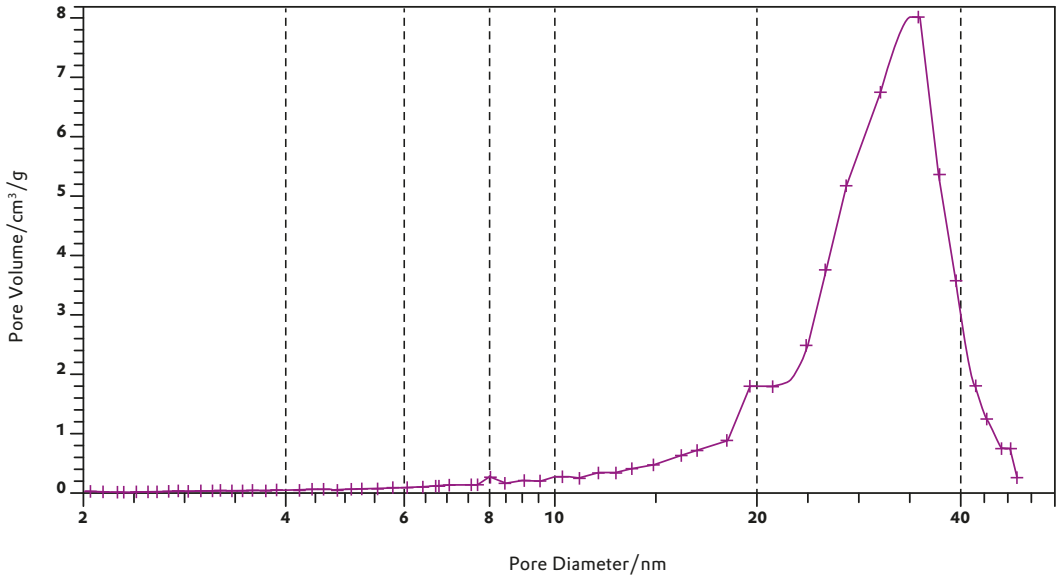


FIGURE 8: POROSITY OF AEROPERL® 300 PHARMA

Measured by nitrogen desorption according to the BJH method. The overall mesopore volume is 1.5 to 1.9 ml/g.



Literature

Granules on the basis of pyrogenic silica, process for their preparation and use thereof, European patent EP 725037.

Use of granular materials based on pyrogenically produced silicon dioxide in pharmaceutical compositions, European patent EP 1439858.

3. AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide: the difference to other silicon dioxide types

Silica produced by flame hydrolysis such as AEROSIL® and AEROPERL® are tested against the regulatory quality requirements of monographs "Colloidal Silicon Dioxide" (USP/NF), "Silica, Colloidal Anhydrous" (Ph. Eur., monograph 434), "Light Anhydrous Silicic Acid" (JP) and "Colloidal Silicon Dioxide" (IP). Next to this type of silica some pharmacopoeia also cover other types of silicon dioxide. Among them are monographs for silicon dioxides used in medicinal toothpaste (USP/NF: "Dental Type Silica", Ph. Eur. monograph 1562: "Silica, Dental Type"), monographs for silicon dioxide produced by precipitation (USP/NF: "Silicon Dioxide", Ph. Eur. monograph 738: "Silica, Colloidal Hydrated") as well as diatomaceous earths (USP/NF: "Purified Siliceous Earth"). These silica are either mined, or produced by precipitation of an alkali silicate solution.

The different process used in the production of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide compared to silicon dioxide tested against the other monographs results in different particle structures and purity. As AEROSIL® Pharma colloidal silicon dioxide products are made in high temperature gas phase processes starting from distilled high purity precursors the materials have a very high chemical purity with exceptionally low elemental contaminations and water content. The typical particle structure of AEROSIL® Pharma colloidal silicon dioxide also provides for high efficiency if used as a glidant and a rheological additive in semi-solid formulations.

Only the AEROSIL® and AEROPERL® fumed silica products identified by the suffix "Pharma" are manufactured according to the GMP guidelines of the International Pharmaceutical Excipients Council (IPEC) for pharmaceutical excipients. Full traceability of all raw materials and production conditions and stringent observance of hygiene protocols during bag filling are guaranteed. Only for the products identified as "Pharma", the quality is checked against the requirements of the main pharmacopoeia and certified by appropriate certificates of analysis. Regulatory and technical support for topics typical for pharmaceuticals such as audits, certifications and access to drug master files is only available for products identified as "Pharma".

4. Product safety and regulatory information

AEROSIL® Pharma colloidal silicon dioxide has been safely used as a pharmaceutical excipient for over 40 years. Current good manufacturing practices as defined for inert pharmaceutical excipients by International Pharmaceutical Excipients Council (IPEC) are followed during the production of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide. As for all excipients, however, it is the ultimate responsibility of the pharmaceutical manufacturer to determine the suitability of AEROSIL® or AEROPERL® Pharma colloidal silicon dioxide as an excipient in a particular formulation.

4.1 PRODUCT SAFETY INFORMATION

AEROSIL® Pharma colloidal silicon dioxide is not harmful when administered orally or topically. It is not irritating to skin and eyes, and is unlikely to be absorbed from the gastrointestinal tract in significant amounts. However, it should not be administered parenterally, because untoward tissue reactions or the formation of granulomas could occur.[6] Unlike crystalline silica, synthetic amorphous AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide does not cause silicosis. However, it is not recommended for drug delivery by inhalation. AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide is inert toward most active drug ingredients and excipients. Adsorption of active components is possible, however the amounts are typically low and the process is reversible.[7]

The surface modification process of the hydrophobic AEROSIL® R 972 Pharma (see Section 2.2) does not significantly affect the toxicological properties of the parent silica.

Before working with any product, read its Safety Data Sheet carefully. Safety Data Sheets (also known as MSDS) for AEROSIL® Pharma products are available for many countries and in different languages. Safety data sheets are available from your local Evonik customer service representative or from our website (www.aerosil.com).

Table 9
Toxicological data for hydrophilic AEROSIL® 200 Pharma, AEROSIL® 200 VV Pharma, AEROSIL® 300 Pharma and AEROPERL® 300 Pharma

Test	Result
Acute oral toxicity, rat	LD50 > 10.000 mg/kg
Acute inhalation toxicity, rat	LC_0= 0.139 mg/l/4 h (maximum attainable concentration in air). No death occurred
Acute dermal toxicity, rabbit	LD50 > 5.000 mg/kg bw
Eye irritation, rabbit	not irritating
Skin irritation, rabbit	not irritating
Genotoxicity (in vitro/in vivo)	No evidence of genotoxic potential
Repeated dose toxicity	No significant toxicity
Carcinogenicity	No evidence of carcinogenic potential
Reproductive toxicity	No findings
Human experience	Silicosis or other substance related illnesses were not observed

Table 10
Toxicological data for hydrophobicAEROSIL® R 972 Pharma

Test	Result
Acute oral toxicity, rat	LD50 > 5.000 mg/kg bw
Acute inhalative toxicity, rat	LC_0= 0.477 mg/l/4 h (maximum attainable concentration in air). No death
Eye irritation, rabbit	not irritating
Skin irritation, rabbit	not irritating
Genotoxicity (in vitro)	No evidence of genotoxic potential
Repeated dose toxicity	No significant toxicity
Carcinogenicity	No evidence of carcinogenic potential
Reproductive toxicity	No findings
Human experience	Silicosis or other substance related illnesses were not observed

[6] A. Wade, P. J. Weller (Eds.), Handbook of Pharmaceutical Excipients, 2nd Edition, American Pharmaceutical Association, Washington, The Pharmaceutical Press, London, 1994
[7] On the adsorption of drug substances on AEROSIL® in tablets (in German). Gstirner, E., Knipp, J. Pharmazeutische Industrie 24 (1962) 475-48

4.2 PHARMACEUTICAL REGULATORY STATUS

Table 11 lists the compendial compliance of all AEROSIL® and AEROPERL® Pharma pharmaceutical grade products.

Table 11
Compendial compliance of pharmaceutical grade AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide products

Product	Tapped Density (in g/L)	DMF (Type IV)	Important Pharmacopoeia Monographs Fulfilled	Comments
AEROSIL® 200 Pharma	approx. 50	1115	• Silica, Colloidal Anhydrous (Ph. Eur.) • Colloidal Silicon Dioxide (USP/NF) • Light Anhydrous Silicic Acid (JP) • Colloidal Silicon Dioxide (IP)	
AEROSIL® 200 VV Pharma	approx. 120	1115	• Silica, Colloidal Anhydrous (Ph. Eur.) • Colloidal Silicon Dioxide (USP/NF)	Generally fulfills JP except for the volume test. No JP or JPE testing is performed
AEROSIL® 300 Pharma	approx. 50	1115	• Silica, Colloidal Anhydrous (Ph. Eur.) • Colloidal Silicon Dioxide (USP/NF)	
AEROSIL® R 972 Pharma	approx. 50	1115	• Silica, Hydrophobic Colloidal (Ph. Eur.) • Hydrophobic Colloidal Silica (USP/NF)	No JP monograph for hydrophobic silica exists at this time.
AEROPERL® 300 Pharma	approx. 270	1115	• Silica, Colloidal Anhydrous (Ph. Eur.) • Colloidal Silicon Dioxide (USP/NF)	Generally fulfills JP except for the volume test. No JP or JPE testing is performed

Table 12
Chemical substance inventory status of AEROSIL® Pharma products

Product	CAS No.	Chemical name	Australia AICS	Canada DSL	China IECSC	Europe EINECS
AEROSIL® 200 Pharma	112945-52-5 resp. 7631-86-9	Silicon dioxide, chemically prepared	registered	registered	registered	231-545-4
AEROSIL® 200 VV Pharma						
AEROSIL® 300 Pharma						
AEROPERL® 300 Pharma						
AEROSIL® R 972 Pharma	68611-44-9	Silane, dichlorodi-methyl-, reaction products with silica	registered	registered	registered	271-893-4

All our pharma products are included in our Type IV Drug Master File (DMF) 1115 for inactive ingredients registered with the US Food and Drug Administration (FDA). Drug master files for inactive ingredients (excipients) are completely confidential and do not have an open part. Upon request, we can issue a Letter of Authorization to the FDA for consideration of DMF 1115 in a customer's new drug application (NDA or ANDA).

Colloidal silicon dioxide is included in the FDA Inactive Ingredients Guide. Please note that the FDA lists all silica products irrespective of the individual monograph under "Silicon Dioxide" in the web-based database (IIG[8]). No maximum daily allowance has been defined for AEROSIL® or AEROPERL® Pharma colloidal silicon dioxide by the FDA or any other regulatory body.

Europe REACH	Europe C&L Inventory	Japan ENCS	Korea KECI	New Zealand NZIoC	Philippines PICCS	USA TSCA
registered	notified	1-548	KE-30953 (KE-31-032)	registered	registered	registered
exempted	exempted	1-548/7-476	KE-10116	registered	registered	registered

[8] Available at http://www.accessdata.fda.gov/scripts/cder/iig/getiigWEB.cfm

4.3 OTHER REGULATORY TOPICS

AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide is completely inorganic in nature. The production process does not involve plant or animal based raw materials, nor does it involve organic solvents. Standard statements are available on request containing information on BSE/TSE, GMO as well as on other criteria. Kosher and Halal Certificates are available upon request; please contact us.

4.4 MICROBIAL CONTAMINATION

Because of the high production temperatures, all AEROSIL® Pharma colloidal silicon dioxide products are sterile immediately after manufacture. It has been reported in the literature that AEROSIL® Pharma colloidal silicon dioxide is not a source of microbial nutrition and that both gram-negative and gram-positive bacteria are unable to survive on dry AEROSIL® Pharma colloidal silicon dioxide for more than hours to days, depending on the type of bacteria.[9] The possible survival of some sporogenic microorganisms cannot be completely ruled out even under these conditions.

The pharmaceutical grades are packaged and stored in accordance with IPEC's GMP guidelines for bulk pharmaceutical excipients. Microbiological testing is performed on random samples at regular intervals. Full pallets are shrink-wrapped to prevent contamination. We, and our partners along the logistics chain, do all that we can to ensure that AEROSIL® Pharma colloidal silicon dioxide reaches our customers without contamination. However, the unexpected can occur during shipping and storage so we recommend customers perform microbiological checks on the product before using it.

4.5 PACKAGING AND STORAGE

AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide are packaged and shipped in multi-ply bags, weights vary according to the product and region. Full pallets are shrink-wrapped at the factory. AEROSIL® Pharma colloidal silicon dioxide is available in FIBC (flexible intermediate bulk container) as well.

AEROSIL® and AEROPERL® Pharma are chemically stable silicon dioxides that could theoretically be stored for many years without any change in their composition. However, because of their large specific surface area they can adsorb volatile substances and moisture from the environment. Proper storage is critical to prevent external contamination of the bags (for example through dust, dirt, or mold). Bags should be inspected thoroughly before opening to prevent contamination of the product.

We recommend that AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide be stored in a dry place, in sealed containers protected from volatile substances, and that they be used within two years after its date of manufacture. We also recommend that the shrink wrapping not be completely removed from the pallet, but that an opening be cut to remove only those bags immediately required, and that the opening be resealed.

[9] The behavior of bacteria in highly pure silica acid (in German) Kienholz, M., Pharmazeutische Industrie, 32 (1970) 677-679

4.6 HANDLING

Evonik has a team of engineers dedicated to improving the handling of AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide in our customers' facilities. With proper equipment AEROSIL® and AEROPERL® Pharma products can be handled almost completely dust-free. For more information on these services, please request our Technical Bulletin Fine Particles No. 28 "The Handling of Synthetic Silica and Silicate".

Even though AEROSIL® and AEROPERL® colloidal silicon dioxide are inert and non-toxic material, there are certain precautions that we recommend because, although not required, they improve the comfort level of persons working with it:

- The work area should be properly ventilated. In the laboratory, work with AEROSIL® and AEROPERL® Pharma products in a fume hood. Where ventilation is not available, a dust respirator is recommended at higher concentrations.
- Avoid continued excessive inhalation by using personal protective equipment.
- Wear appropriate eye protection.
- Wash hands after handling AEROSIL® and AEROPERL® Pharma products as the product may leave a dry feeling on the skin. Use of protective skin cream and/or gloves is recommended when working with AEROSIL® and AEROPERL® products.
- See the Product Safety Data Sheet for information relevant to maximum work area concentrations and other safety aspects of our products.

In addition, for safety reasons it should be noted that all dry powders such as AEROSIL® and AEROPERL® colloidal silicon dioxide can build up static electrical charges when subjected to friction during conveyance and/or mixing. When handling AEROSIL® colloidal silicon dioxide near flammable or explosive liquids, be sure to take proper safety precautions, such as electrical grounding, inert atmosphere, etc. For further information, please request our Technical Bulletin Pigments No. 62 Synthetic Silica and Electrostatic Charges.

Besides this Technical Information, other publications on AEROSIL® and AEROPERL® Pharma colloidal silicon dioxide are freely available on our website www.aerosil.com.

EUROPE/MIDDLE-EAST/ AFRICA

Evonik Resource Efficiency GmbH
Business Line Silica
Rodenbacher Chaussee 4
63457 Hanau-Wolfgang
Germany

Phone +49 6181 59-12532
Fax +49 6181 59-712532

ask-si@evonik.com
www.evonik.com

NORTH AMERICA

Evonik Corporation
Business Line Silica
299 Jefferson Road
Parsippany, NJ 07054-0677
USA

Phone +1 800 233-8052
Fax +1 973 929-8502
ask-si-nafta@evonik.com

ASIA / PACIFIC

Evonik (SEA) Pte. Ltd.
Business Line Silica
3 International Business Park
#07–18 Nordic European Centre
Singapore 609927

Phone +65 6 809-6877
Fax +65 6 809-6677
ask-si-asia@evonik.com

RE-139-NOV16L+L

EVONIK
POWER TO CREATE