

Impact of mesoporous silica on the chemical degradation of Praziquantel upon grinding

Ivana Šagud^{1§}, Debora Zanolla^{2§}, Guglielmo Zingone², Beatrice Perissutti^{2*} and Irena
Škorić^{3*}

¹Pliva Tapi R&D, TEVA, Prilaz Baruna Filipovića 25, 10000 Zagreb, Croatia

²Department of Chemical and Pharmaceutical Sciences, University of Trieste, P.le Europa 1,
34127 Trieste, Italy

³Department of Organic Chemistry, Faculty of Chemical Engineering and Technology,
University of Zagreb, Marulićev trg 19, 10000 Zagreb, Croatia

§ These authors contributed equally.

**Corresponding authors.*

iskoric@fkit.hr; +385-1-4597241 (Irena Škorić)

bperissutti@units.it; +39-040-5583106 (Beatrice Perissutti)



TO WHOM IT MAY CONCERN

Grace GmbH
In der Hollerhecke 1, 67547 Worms
Tel: ++49-(0)-6241 403 1302
Fax: ++49-(0)-6241 403 90 1302
E-mail: Ramona.Eberle@grace.com

07 Nov 2017
201720485

Certificate of Analysis

Inspection Certificate (DIN EN 10204-3.1)

Your order no.
Our order no. SAMPLE
Product SYLOID 244 FP S/P/F 010/140
Batch no. 1000314703
Production date 25/09/2017

This batch conforms to the specification as published in the latest editions by USP/NF for Silicon Dioxide, EP for Silica, Colloidal Hydrated and the JPE for Hydrated Silicon Dioxide. It meets the requirements for Sulfate <0.5 %; Cl<=0.1%; Substances soluble in HCl <2.0%; Water-adsorption capacity 'remains powdery'; HM<=25mg/kg; As<=0.5mg/kg; Pb<=2mg/kg; and Hg<=0.1mg/kg. Testing is performed minimum on a semi-annual basis. It fulfills the guidelines for avoiding unnecessary testing of Organic Volatile Impurities, USP/NF Method IV (467) because no organic solvents are used for production. Meets food additive standards: FCC; Regulation (EU) No. 231/2012 for E551. Samples of the above mentioned batch no. have been analysed and the following average data were obtained:

<u>Test name</u>	<u>Unit</u>	<u>Result</u>	<u>Specification</u>		<u>Test method</u>
			<u>min.</u>	<u>max.</u>	
Wet Screen Residue > 25 Micron	%	<0,01		0,01	Q 004
pH-value (USP)	.	7,5	6,0	8,0	Q 011
Average Particle Size (Malvern)	(µm)	3,1	2,5	3,7	Q 013
SiO ₂ (ignited base)	%	99,2	99,0		Q 046
Loss on Drying (USP)	%	2,8		5,0	Q 047
Loss on Ignition	%	3,5		8,5	Q 048
pH-value (EP)	.	5,46	4,00	7,00	Q 218
Fe ₂ O ₃	%	0,009		0,020	Q 271

Recommended retest date: 12 months after production.

R. Eberle; Administrator Quality Control

Product Information

SYLOID® 244 FP

Food Additive and Pharmaceutical Excipient

Product Description

SYLOID® 244 FP Food Additive and Pharmaceutical Excipient is a synthetic amorphous silica appearing as a white free flowing powder. It has a very high purity and is taste and odor free. It meets the test requirements as published in the latest editions by U.S. Pharmacopoeia-National Formulary for Silicon Dioxide, European Pharmacopoeia for Silica, Colloidal Hydrated, and Japanese Pharmaceutical Excipients for Hydrated Silicon Dioxide. It also meets food additive standards, such as Food Chemical Codex (FCC); Regulation (EU) No. 231/2012 for E 551; Japan's Specification on Standard for Food Processing Aids (D325).

Product Characteristics

The following specification parameters are the criteria of acceptance and will be stated on our Certificate of Analysis.

Property	UOM	Value	Test Method
Loss on Drying (USP, 145°C, 4 h)	%	5.0 max.	GRACE Q 047
Loss on Ignition (1000°C, 1 h)	%	8.5 max.	GRACE Q 048
Average Particle Size - Malvern® Mastersizer® 2000	µm	2.5 - 3.7	GRACE Q 013
Wet Screen Residue (> 25 µm)	%	0.01 max.	GRACE Q 004
pH (5 % aqueous suspension)		6.0 - 8.0	GRACE Q 011
pH (EP)		4.0 - 7.0	GRACE Q 218
Assay (SiO ₂ , ignited basis)	%	99.0 min.	GRACE Q 046
Fe ₂ O ₃ Content (dry basis)	%	0.02 max.	GRACE Q 271

When retesting, the parameter „Loss on Drying” should be analysed.

Typical Properties and Recommended Applications

The following Typical Properties data are given for informational purposes only, and are not to be interpreted as product or in-process specifications.

Property	Unit	Typical Value	Test Method
Pore Volume (N ₂)	ml/g	1.6	GRACE Q 049
Oil Adsorption	g/100 g	300	GRACE Q 015

SYLOID® 244 FP Food Additive and Pharmaceutical Excipient is a fine-sized, high pore volume silica gel with a large internal surface area. Its strong affinity for moisture along with its ease of incorporation can effectively contribute to the processability, stability and shelf life of products in many pharmaceutical and food applications. Key features are:

- Multifunctional additive, excellent compatible with active ingredients
- Highly adsorptive as carrier for liquids and actives, up to 1.6 ml of a liquid per gram
- Can keep powders dry and free flowing for a more consistent and uniform processing / dosing
- Can be highly efficient as inactive excipient for improving oral formulations especially of moisture-sensitive pharmaceutical active ingredients

www.grace.com

GRACE®, Talent | Technology | Trust™, and SYLOID®, SYLOBLOC®, SYLOBLANC®, SYLODENT®, SYLOJET®, SHIELDEX®, DARACLAR®, TRISYL®, DAVISIL® are trademarks,

registered in the United States and/or other countries, of W. R. Grace & Co.-Conn.

MALVERN® and MASTERSIZER® are registered trademarks of Malvern Instruments, Limited.

This trademark list has been compiled using available published information as of the publication date of this Product Information Sheet and may not accurately reflect trademark ownership or status.

Grace Materials Technologies is a business unit of W. R. Grace & Co.-Conn.

© Copyright 2016 W. R. Grace & Co.-Conn.

Packaging Information

The standard packaging for SYLOID® 244 FP Food Additive and Pharmaceutical Excipient is:

10 kg/bag 14 bags/pallet 140 kg/pallet pallet: 1000 x 1200 mm

Handling & Storage Recommendations

Like all other finely powdered products SYLOID® 244 FP Food Additive and Pharmaceutical Excipient has a tendency to develop dust. During handling, precautions should be taken against electrostatic discharges. SYLOID® 244 FP Food Additive and Pharmaceutical Excipient should be stored in a clean, dry warehouse to protect against moisture and contamination. Its high adsorptive capacity necessitates keeping it separately from odors, organic solvents, and odorant materials during transportation, storage and handling. The material stored in GRACE's original standard packaging on the pallet under GRACE's storage recommendations will meet its specifications for 12 months after the date of production, the material in special packaging (available on request) for 24 months after the date of production. After this period of time GRACE's warranty ends. Use of the product after the end of the warranty period is solely at your discretion. If the silica gel is stored beyond the end of the warranty period and you should decide to use the product at such time, it is recommended that you perform a quality test according to the given retest parameters. Grace disclaims all liability for performance of the product after the end of the warranty period.

Health & Safety Information

SYLOID® 244 FP Food Additive and Pharmaceutical Excipient is synthetic, amorphous silica, which is manufactured and handled by GRACE according to HACCP concept, considering the requirements of this standard. Additional information can be found in our Safety Data Sheet (SDS). Please refer also to national laws and regulations.

Certifications

- DIN EN ISO 9001
- DIN EN ISO 14001
- DIN EN ISO 50001
- EXCIPACT™ - GMP/GDP

Other Information

The information contained herein is based on our testing and experience and is offered for the user's consideration, investigation and verification. Since operating and use conditions vary and since we do not control such conditions, we must **DISCLAIM ANY WARRANTY, EXPRESSED OR IMPLIED**, with regard to results to be obtained from the use of this product. Test methods are available on request.

Contact

World Headquarters

W. R. Grace & Co.-Conn.
7500 Grace drive
Columbia, Maryland 21044 USA
Tel.: +1 410.531.4000
NA Toll Free: +1 800.638.6014
Fax: +1 410.531.4273

Latin America

W.R. Grace Brasil Ltda.
Avenida Rio Negro, 500
-Torre B - sala 2201
Alphaville, Barueri, Sao Paulo,
Brazil 06454-000
Tel: +55.11.4197.7540

Europe

Grace GmbH & Co. KG
in der Hohenmecke 1
67547 Worms/Germany
Tel: +49.6241.403.00
Fax: +49.6241.403.1211

Asia/Pacific

Grace Trading (Shanghai) Limited
1010 Huai Hai Zhong Road
19th Floor, K Wah Centre
Shanghai, 200031/China
Tel: +86.21.3325.8288
Fax: +86.21.5405.1500

www.grace.com

GRACE®, Talent I Technology I Trust™, and SYLOID®, SYLOBLOC®, SYLOBLANC®, SYLODENT®, SYLOJET®, SHIELDX®, DARACLAR®, TRISYL®, DAVISIL® are trademarks, registered in the United States and/or other countries, of W. R. Grace & Co.-Conn. MALVERN® and MASTERSIZER® are registered trademarks of Malvern Instruments, Limited.

This trademark list has been compiled using available published information as of the publication date of this Product Information Sheet and may not accurately reflect trademark ownership or status.

Grace Materials Technologies is a business unit of W. R. Grace & Co.-Conn.
© Copyright 2016 W. R. Grace & Co.-Conn.



Grace GmbH
 In der Hollerhecke 1
 67547 Worms
 Germany
 Telefon: (0 62 41) 40300
 Telefax: (0 62 41) 403-211

88826175

Requested Delivery Date: 11.12.2017

Ship To
UNIVERSITA' DI TRIESTE
DIPARTIMENTO CHIMICA E FARMACEUTICA
ATT: DR.SSA BEATRICE PERISSUTI
PIAZZALE EUROPA 1
I-34127 TRIESTE TS

Delivery Area:
11/12/2017

Our order no.	
6177894	27.11.2017
Your Contact	
LZAGO 00390293148829/	
Your order no.	
UNIV. TRIESTE-PERISSU	
Shipping document	
88826175	11.12.2017
Shipped From	
Worms Samples - Davison	
Carrier	
UNIVERSITA' DI TRIESTE	
Terms of Delivery	
CPT Destination	
Sold-to	Vat No.
551942	
Freight Terms	
Terms of payment	

Requested Delivery Date: 11.12.2017

Description	Ordered Qty	Dispatch. Qty Net	Dispat. Qty Gross	Batch
-------------	-------------	-------------------	-------------------	-------

SYLOID 244 FP 5080425	SAMPLE 1,5L/0,15 1 CAN	HS Code:28112200	1 CAN	0,350 KG	1000314703
---------------------------------	----------------------------------	------------------	-------	----------	------------

Net Weight: 0,15 KG **Gross Weight: 0 KG**

The Order has been Completely Delivered

Please refer to our Material Safety Data Sheets and Product Information Sheets

We confirm that all deliveries of the above product were taken from material which has been tested and found to conform to the agreed product specifications.

Grace GmbH
 Amtsgericht Mainz HRB 47549
 Steuernummer 44/678/1113/1
 Geschäftsführer: Robin F. Pearce (Vors.), Stephen W. Addison