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Sartocheck® 4 | Sartocheck® 4 plus Automatic Detection of Improper Test Setup

Application Note

Filter Integrity Testing

turning science into solutions

Dr. Jens Meyer
Gary Dawson
Martin Dahlberg

Background Information

Filter integrity testing is a crucial requirement in biopharmaceutical production processes. Automatic test units perform indirect tests to verify the pore size to be as specified for a sterilizing-grade membrane filter. Different test methods are established for which a specific test pressure is applied to a wetted membrane. In most cases self-closing quick connectors (e.g. Stäubli couplings) are used for pneumatic connection of the test tubing from the integrity tester to the test housing. In case of an inadvertently disconnected filter housing, the normally-closed coupling will cause the test unit to only pressurize the internal test tubing and not the filter housing. In that situation, the integrity tester will not detect any significant diffusion rate or any relevant nonlinearity in flow, which is needed to detect the bubble point. However, as the only criteria for the test evaluation, a maximum diffusion rate and | or minimum bubble point is defined. Both criteria (max. diffusion rate is not exceeded and bubble point is greater than minimum BP) might be fulfilled when only the tubing is tested. In that situation an integrity test without any filter might be classified as "test passed," which indeed is a false positive test result.

An experienced operator may immediately recognize the "flatline" of the BP or diffusion curve. Nevertheless, there is a remaining risk for the daily routine work. This application note describes a new feature of the Sartocheck® 4 and Sartocheck® 4 plus which increases the detection capability of the integrity testing procedure by identifying an improper test setup.

How to Avoid False Positive Test Results?

In contrast to previous versions, the latest software version of Sartocheck® 4 (version 2.03) and Sartocheck® 4 plus has added three independent parameters that provide the enhanced detection of an incorrect test set up. The proper use of these parameters will reliably detect situations in which the test set up is not pneumatically connected to the integrity tester, or if a blind end cap or pinched line is preventing normal air flow.

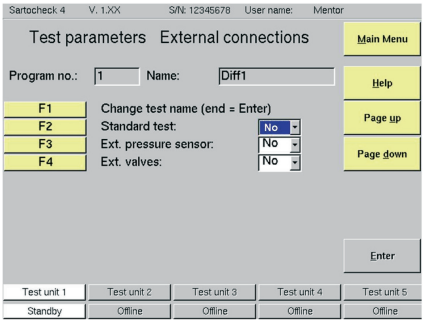
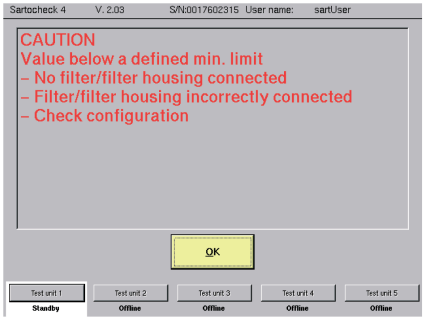


Figure 1:
Screenshot of Sartocheck® 4 that shows how to activate the additional parameters: a non-standard test has to be chosen.

To preserve the well established foundation of the test pass | fail status, the criteria used to define the outcome of the tests have not been changed. However, when an improper test setup is detected, an additional warning message will subsequently be displayed and printed in red with the



following text:
Figure 2:
Screenshot of Sartocheck® 4 showing the warning message that is displayed if an incorrect test setup is detected.

The following parameters to detect an improper test set up can be entered by the user:

Min. Diffusion
(for the Diffusion, WIT and WFT tests)
This parameter defines a realistic minimum diffusion rate that would be expected for a filter that is properly connected to the Sartocheck® (there must be some amount of expected diffusion if a filter is connected).

Min. Net Volume (for all tests that include volume determination step)
This parameter defines the minimum upstream volume of the test setup (tubing plus filter capsule or filter housing). A test set up connected to the Sartocheck® via the test tubing will have a specific net upstream volume. A disconnected filter (or filter housing) will result in an inordinately low upstream volume that only reflects the internal tubing of the Sartocheck unit itself.

Min. Flow BP Test
(for the Bubble Point test only)
This parameter defines the diffusive flow rate just prior to reaching BP_{max}. A disconnected filter (or filter housing) will result in an inordinately low flow rate.

The concept behind these three parameters is that as soon as any filter housing is connected to the Sartocheck, and a test is started, an increased net volume and a significant diffusion rate should be measured. To cover all possible conditions, all three parameters are required.

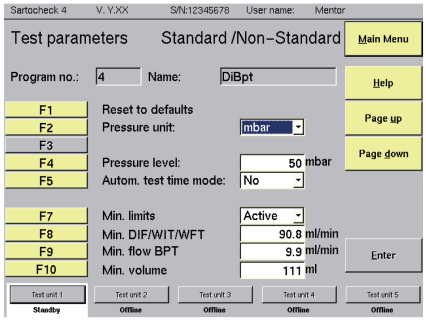


Figure 3:
Screenshot of the Sartocheck® 4 (version 2.03) which shows where the additional parameters are defined.

Adjusting the parameters
These three parameters have been implemented to detect a situation in which a filter (housing or capsule) has not been properly connected to the Sartocheck®. As such, these parameters should be programmed to distinguish between the situations of a "filter connected" and "no filter connected." Because the respective flow rates and net volumes are dependent upon on the individual test setup, no predetermined values can be recommended. Rather, the general recommendations for selecting the optimal values are as follows:

Minimum Diffusion:
Acquire the "blind diffusion" (in mL/min.) by running a diffusion test with no test setup connected. This measured diffusion can be used as Minimum Diffusion value. This value should always be very low (something around 3 or 4 mL/min.) and should never be near the true diffusion of a passing filter cartridge to avoid false error messages.

Minimum Flow BPT:
The parameter min diffusion BP test is the diffusion rate that is measured just before reaching the Max. BP pressure. As such, a good rule for defining this value is using ½ of the $Diff_{max}$ value.

Minimum Net Volume:
This value should be programmed within 80 – 90% of the actual net upstream volume of the housing with the filter installed, or the upstream volume of the filter capsule (if no housing is used). For example: If the SC4 measures a net upstream volume of 1000 mL for a given test setup, then a Minimum Net Volume of 850 mL should be programmed. The only requirement is to define a value that lies between the respective volumes for a decoupled test set up, and the net volume of a properly connected test set up, respectively. This is typically a very broad range, making the Minimum Net Volume very easy to define somewhere in between the two extremes.

The Sartocheck® 4 allows the choice of either activating or deactivating the new safety parameters. However, in case of a decoupled test setup, this condition will only be reliably identified when the parameters are activated:

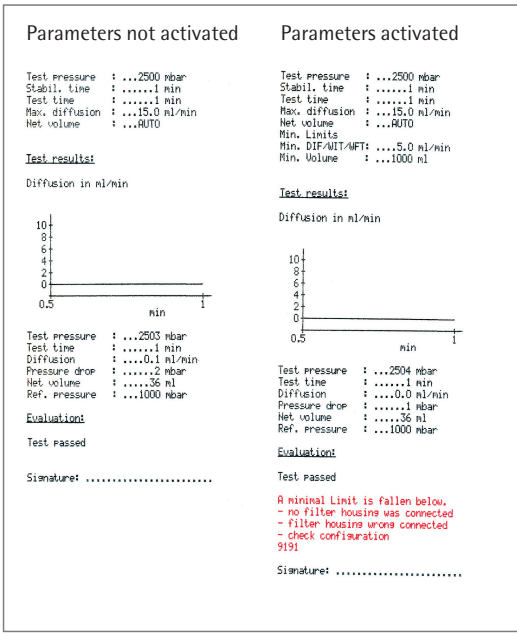


Figure 4:
Printouts of Sartocheck® 4 with deactivated (left) and activated (right) safety parameters. A diffusion test was performed with a disconneted test tubing. This condition was only identified when the new parameters were activated, resulting in a warning message displayed on the screen and printed in red.

Conclusion:
The new detection features of Sartocheck® 4 (≥ software version 2.03) and Sartocheck® 4 plus significantly increase the robustness of filter integrity testing. When those additional three parameters (Min. Diffusion, Min Flow BPT, and Min Net Volume) are defined correctly, the Sartocheck® reliably eliminates the possibility of false positive test results that might otherwise occur in the daily work routine due to a disconnected or improper test setup.

Sales and Service Contacts

For further contacts, visit www.sartorius-stedim.com

Europe

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen

Phone +49.551.308.0
Fax +49.551.308.3289

www.sartorius-stedim.com

Sartorius Stedim Systems GmbH
Schwarzenberger Weg 73–79
34212 Melsungen

Phone +49.5661.71.3400
Fax +49.5661.71.3702

www.sartorius-stedim.com

France
Sartorius Stedim Biotech S.A.
ZI Les Paluds
Avenue de Jouques – BP 1051
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.845619

Sartorius Stedim France SAS
ZI Les Paluds
Avenue de Jouques – CS 71058
13781 Aubagne Cedex

Phone +33.442.845600
Fax +33.442.846545

Austria
Sartorius Stedim Austria GmbH
Franzosengraben 12
A-1030 Vienna

Phone +43.1.7965763.18
Fax +43.1.796576344

Belgium
Sartorius Stedim Belgium N.V.
Leuvensesteenweg, 248/B
1800 Vilvoorde

Phone +32.2.756.06.80
Fax +32.2.756.06.81

Denmark
Sartorius Stedim Nordic A/S
Hoerskaetten 6D, 1.
DK-2630 Taastrup

Phone +45.7023.4400
Fax +45.4630.4030

Italy
Sartorius Stedim Italy S.p.A.
Via dell'Antella, 76/A
50012 Antella-Bagno a Ripoli (FI)

Phone +39.055.63.40.41
Fax +39.055.63.40.526

Netherlands
Sartorius Stedim Netherlands B.V.
Edisonbaan 24
3439 MN Nieuwegein

Phone +31.30.6025080
Fax +31.30.6025099

Spain
Sartorius Stedim Spain SA
C/Isabel Colbrand 10,
Oficina 70
Polígono Industrial de Fuencarral
28050 Madrid

Phone +34.90.2110935
Fax +34.91.3589623

Switzerland
Sartorius Stedim Switzerland GmbH
Lerzenstrasse 21
8953 Dietikon

Phone +41.44.741.05.00
Fax +41.44.741.05.09

U.K.
Sartorius Stedim UK Limited
Longmead Business Park
Blenheim Road, Epsom
Surrey KT19 9 QQ

Phone +44.1372.737159
Fax +44.1372.726171

America

USA
Sartorius Stedim North America Inc.
5 Orville Drive
Bohemia, NY 11716

Toll-Free +1.800.368.7178
Fax +1.631.254.4253

Sartorius Stedim SUS Inc.
1910 Mark Court
Concord, CA 94520

Phone +1.925.689.6650
Toll Free +1.800.914.6644
Fax +1.925.689.6988

Sartorius Stedim Systems Inc.
201 South Ingram Mill Road
Springfield, MO 65802

Phone +1.417.873.9636
Fax +1.417.873.9275

Argentina
Sartorius Argentina S.A.
Int. A. Avalos 4251
B1605ECS Munro
Buenos Aires

Phone +54.11.4721.0505
Fax +54.11.4762.2333

Brazil
Sartorius do Brasil Ltda
Av. Dom Pedro I, 241
Bairro Vila Pires
Santo André
São Paulo
Cep 09110-001

Phone +55.11.4451.6226
Fax +55.11.4451.4369

Mexico
Sartorius de México S.A. de C.V.
Circuito Circunvalación Poniente No. 149
Ciudad Satélite
53100 Naucalpan, Estado de México

Phone +52.5555.62.1102
Fax +52.5555.62.2942

Asia | Pacific

China
Sartorius Stedim Beijing
Representative Office
No. 33, Yu'an Road,
Airport Industrial Zone B, Shunyi District
Beijing 101300

Phone +86.10.80426516
Fax +86.10.80426580

Sartorius Stedim Shanghai
Represantative Office
Room 618, Tower 1, German Centre,
Shanghai, PRC., 201203

Phone +86.21.28986393
Fax +86.21.28986392.11

Sartorius Stedim Guangzhou Office
Room 704, Broadway Plaza,
No. 233–234 Dong Feng West Road
Guangzhou 510180

Phone +86.20.8351.7921
Fax +86.20.8351.7931

India
Sartorius Stedim India Pvt. Ltd.
10, 6th Main, 3rd Phase Peenya
KIADB Industrial Area
Bangalore – 560 058

Phone +91.80.2839.1963|0461
Fax +91.80.2839.8262

Japan
Sartorius Stedim Japan K.K.
KY Building, 8–11
Kita Shinagawa 1-chome
Shinagawa-ku
Tokyo 140-0001

Phone +81.3.3740.5407
Fax +81.3.3740.5406

Malaysia
Sartorius Stedim Malaysia Sdn. Bhd.
Lot L3-E-3B, Enterprise 4
Technology Park Malaysia
Bukit Jalil
57000 Kuala Lumpur

Phone +60.3.8996.0622
Fax +60.3.8996.0755

Singapore
Sartorius Stedim Singapore Pte. Ltd.
10, Science Park Road, The Alpha
#02-25, Singapore Science Park 2
Singapore 117684

Phone +65.6872.3966
Fax +65.6778.2494

Australia
Sartorius Stedim Australia Pty. Ltd.
Unit 5, 7-11 Rodeo Drive
Dandenong South Vic 3175

Phone +61.3.8762.1800
Fax +61.3.8762.1828

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