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Options for Shortening the Test Time with Sartocheck® 4 plus

Application Note

Filter Integrity Testing

turning science into solutions

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Background Information
The integrity testing of sterile filters constitutes a critical and mandatory regulatory step in biopharmaceutical production processes. However, performing such filter integrity tests costs time. Indeed, it can take a good 20 to 30 minutes to perform a diffusion test, bubble-point test or water intrusion test. For this purpose, it appears desirable to come up with rational options for shortening the test time provided that the proper test results can still be guaranteed.

This application report describes several possible ways to reduce the test time required when using the filter integrity tester Sartocheck® 4 plus by up to 90%.

What Factors Determine the Test Time?
An integrity test is made up of several different test phases. In general, one distinguishes between a stabilization phase and the test phase. As the name suggests, the purpose of the **stabilization phase** is to achieve stabile test conditions. Particularly when pressure is applied at the beginning of the test, e.g. when the tester is pressurized to a programmed test pressure of 2500 mbar, a thermodynamic process takes place: the filter cartridge housing to be tested fills with the test gas (e.g. compressed air) – a process that per se inputs energy into the system. This energy input can be quantified directly in that a temperature increase of as much as several degrees Celsius is measured. After pressurization, the temperature drops again or temperature compensation takes place between the filter cartridge housing and the environment. Since the volume in the filter cartridge housing remains constant, a drop in temperature in the gas-filled housing correspondingly leads to a drop in pressure (pV=nRT). The integrity tester connected to this system cannot differentiate between a pressure drop caused by diffusion and a pressure drop caused by temperature fluctuations. As a result, a shortening of the recommended stabilization time is always associated with the risk of unstable conditions, which can significantly impair the test results. Therefore, it is fundamentally not recommended to substantially shorten the stabilization time just to save time.

In contrast to stabilization phase, however, constant conditions prevail during the subsequent **test phase**. That means that, here, various possibilities arise for shortening the test time. These possibilities will be explained in greater detail in the following:

1. Diffusion Test and Water Intrusion Test
During the diffusion test, the system is stabilized to a filter type-dependent test pressure and then the diffusion taking place is measured for a certain amount of time (typically 10 min) at an unchanged pressure level. Under very stabile conditions, the measurement may not change in any relevant way throughout the entire test. Moreover, it has been found that the real test values obtained on filter cartridges are usually far within the permissible limit values. This fact begs the question as to whether it is really necessary to wait until the end of the test when stable conditions prevail much earlier (i.e. stabile measurements are obtain) and it has already become certain that the measured filter cartridge will pass the test.

The following example serves to illustrate this point: A programmed diffusion test was used to measure a 10" filter cartridge of the type Sartopore® 2 (0.2 µm) at a test pressure of 2500 mbar. Just briefly after the test started, the diffusion stabilized to a mean of 7.3 mL/min (see Figure 1).
The measured values showed a very low spread; the measurement was extremely stable right from the onset. Lastly, one had to wait for the 10-minute test phase to be over to obtain an already confirmed positive test result.

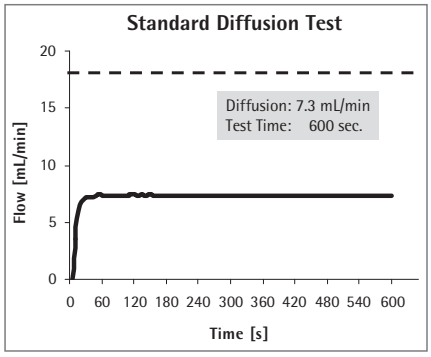

Figure 1:
A diffusion test programmed with standard parameters (10 min test time at 2500 mbar) run on a 10" Sartopore® 2 (0.2 µm) filter cartridge produced a result of 7.3 mL/min. Notably, the test result was already clear right from the start of the test and was very considerably within the tolerances to the limit value (max. diffusion). In such a situation, one must ask whether it is really necessary to wait for the entire 10 minutes' test time.

By considering a logical stability criterion, however, the test time can be shortened significantly. Sartocheck® 4 plus features an option that allows the activation of this kind stability criterion. When the **automatic test time mode** is activated, a test signal is registered as stable, when the mean variation of 10 consecutively measured values is within a defined band (±2%). Once this condition is met, the test terminates early and the device issues the test result "Test passed".

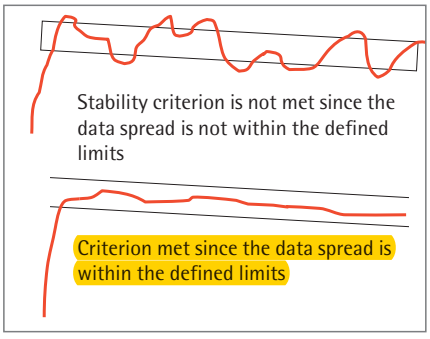

Figure 2:
Schematic illustration of how the stability criterion works in the automatic test time mode.

The following section describes how the diffusion test was repeated on the same filter cartridge using identical test parameters, but with the automatic test time mode activated. In the first trial run, the diffusion test (the test phase) took 10 minutes, whereas it was cancelled after just 65 seconds when run with the automatic test time mode activated (Figure 3). The test was evaluated as passed; the measured diffusion was similarly 7.3 mL/min. Consequently, this means that the test phase can be shortened by 89 % (!) and the test can still produce identical test results. However, the test result doesn't necessarily have to be identical. When the diffusion curve shows a decline, then obviously there will be a higher value at the beginning of the test than towards the end. The important thing in this regard – as mentioned above – is the large tolerance between the real test result and the relevant limit value. This fact demonstrates that shortening the test time still delivers accurate results.

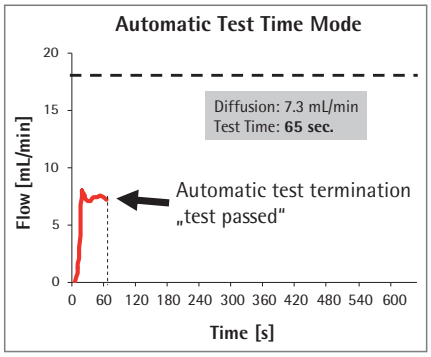

Figure 3:
Diffusion test performed on a Sartopore® 2-type filter cartridge (identical cartridge as in Fig. 1) with the automatic test time mode activated. The test was terminated successfully after just 65 seconds. This is equivalent to shortening the test phase by 89%.

The printout and | or the file with the results indicates that the automatic test time mode was activated, making it instantly apparent to the reader. The automatic test time mode can be used for the diffusion test, water intrusion test and water flow test types.

2. Bubble Point Test

Performing the bubble point (BP) test can also be very time-consuming. The automatic test time mode function is not appropriate for the BP test because its test conditions per se are not really ever stable. Rather, the BP test involves elevating the pressure incrementally until the bubble point criterion has been reached (disproportionate increase in airflow rate). Despite the above, two different means can be employed when performing the BP test that likewise markedly contribute to reducing the test time.

Programming the Maximum Bubble Point

The singular relevant parameter for evaluating the test is the minimum bubble point. The BP test counts as passed as soon as the pressure levels have reached this minimum pressure without the tester detecting the bubble point. As described above for the diffusion test, the real test value is usually far removed from the pre-defined limit value (BPmin). This means that sometimes many pressure levels are reached between the min. BP and the actual BP. Because every pressure level takes up additional time, one can ask whether this information about the actual bubble point is really so imperative. Whenever this is not the case, the test time can be significantly shortened by programming the maximum BP lower. The following example of the tested Sartopore® 2 cartridge aims to provide a clear illustration of this:

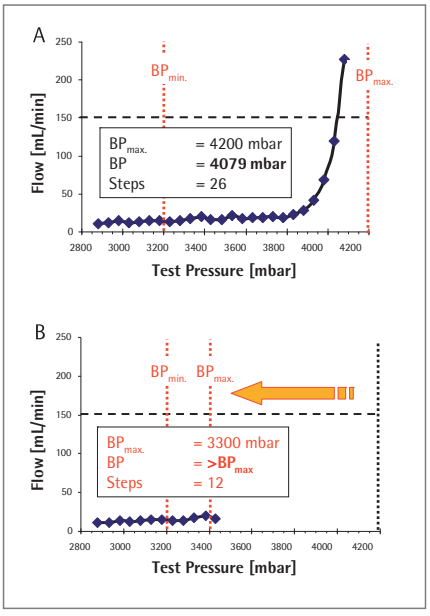

Figure 4:
Shortening the test time on the bubble point test by programming lower values for the maximum bubble point. The diamonds represent the individually measured values (pressure levels).

In the first graphic (Fig. 4A), a BP test was programmed with a BP_{min} of 3200 mbar and a BP_{max} of 4200 mbar. The bubble point was detected at 4079 mbar, which required a total of 26 pressure levels.
In the second graphic (Fig. 4B), the BP_{max} was set low, namely at 3400 mbar. This meant that Sartocheck® 4 plus terminated the test as soon as this BP_{max} was reached and displayed the message "Test Passed, $BP>BP_{min}$". As explained above, the only criterion for evaluating the test is the minimum BP; whereas, the maximum BP is absolutely irrelevant for the test evaluation. Ultimately, the maximum BP only reflects the maximum test pressure at which the test is terminated (successfully). In the example above, only 12 pressure levels were required; this converts to a greater than 50% reduction in the required test time.

It should be noted, however, that any information about the actual bubble point is lost using this method. Here, it is up to the users to decide whether this method is suitable to meet their individual needs or satisfy their internal operating procedures. At any rate, it is legitimate as far as the regulatory requirements are concerned.

Changing the Pressure Levels

As mentioned at the beginning, during the BP test, the test pressure is elevated incrementally until the criterion for BP detection has been reached. In this context, it becomes obvious that it will take longer when the pressure is regulated in smaller increments than if larger increments were used. By doubling the pressure levels, it only takes half the time to achieve the given target pressure.

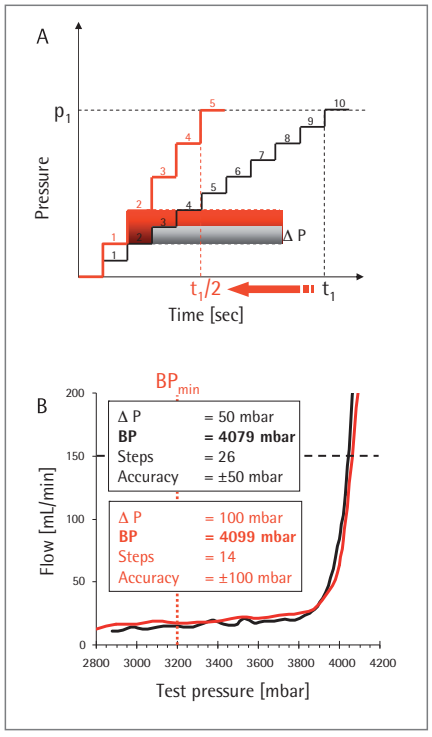

Figure 5:
Changing the pressure levels on the BP test. By doubling the pressure level increment from 50 to 100 mbar, the respectively required pressure is reached in half the test time. This fact was also confirmed by testing a Sartopore® 2 cartridge. The effect of this change on the test result was negligible.

The standard pressure level setting programmed on Sartocheck® testers is 50 mbar. If a non-standard test is selected when programming a test, i.e. the BP test (compare Fig. 6), the pressure level can be selected freely. Whenever that is the case, attention should be paid that the measuring accuracy of ±50 mbar stated in the unit's technical specifications for the BP test only applies to the pre-set pressure levels of 50 mbar. If, for example, the pressure levels are increased up to 100 mbar, then the measuring accuracy is also reduced accordingly to the same ±100 mbar. As illustrated in the example above, this lower measuring accuracy is adequate in most of the cases. Under these circumstances, when the pressure levels are 50 mbar and 100 mbar, the BP is found at 4079 mbar and 4099 mbar (Fig. 5), respectively. In both cases, this is far above the permissible limit value and thus appears acceptable.

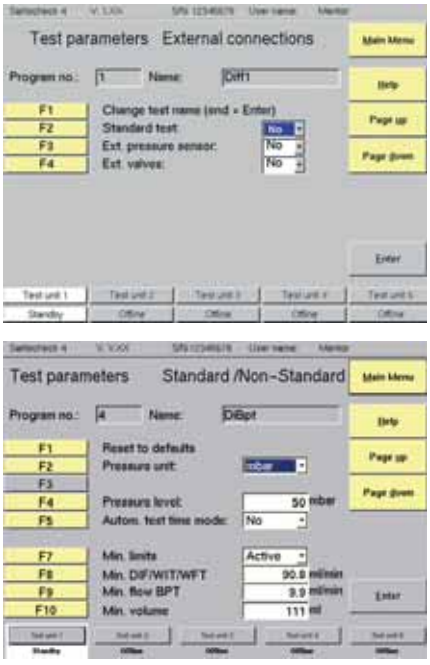

Figure 6:
To activate the different methods for shortening the test time, i.e. using the automatic test time mode for the diffusion test and WIT or changing the pressure levels for the BP test, it is necessary to select a non-standard test. Next, a menu item appears in a window where both the automatic test time mode can be activated and the corresponding BP test pressure level can also be set.

Conclusion

The aim of this paper was to describe the technical possibilities that are feasible options for shortening test times on the Sartocheck® 4 plus integrity tester. In this respect, Sartocheck® 4 plus offers efficient solutions for performing the diffusion, bubble point, water intrusion and water flow tests with markedly shorter test times. The present paper has explained the theoretical background and presented real test results that clearly demonstrated how test times can be significantly shortened by up to between 50 and 90%. Indeed, there are no technical reasons why you should not opt to sensibly employ these methods in your own routine work.

In closing, it is important to note that before employing any of the methods described for shortening test times, you must decide whether it is paramount to achieve the highest possible measuring accuracy or whether your main emphasis is on the fastest possible test times. This decision always presents a conflict that begs an acceptable compromise and must be made by the user himself. In this respect, the Sartocheck® 4 plus integrity tester offers users a broad range of options.

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