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Sterility Testing System The Closed, Reusable System for USP and EP Sterility Testing



turning science **into solutions**

Sterility Testing System – The Closed, Reusable System for USP and

Your Advantages at a Glance

- Eliminates secondary contamination
- Permits sterility testing and incubation, all in one instrument
- Permits individualized set-up according to laboratory requirements
- No transfer, cutting or punching of filter
- Extremely economical
- Environmentally friendly

Effective testing of the sterility of injectable pharmaceutical products has become an essential part of manufacturing and quality control. Pharmacopeias recommend that the membrane filter method be used as the procedure of choice whenever possible (EP4).

For accurate and reproducible results, the elimination of secondary contamination is an absolute must during the sterility testing process. For this reason, the test should be carried out in a clean room environment. Accurate results are also dependent on the choice of filter holder used. According to experience and specific requirements, this holder should be in a closed system that ensures sterility as well as guarantees ease of handling.

The Sartorius sterility testing system fulfills all of the above requirements, and in addition, allows the contents of each sample container to be tested using two or more culture media. Also, the tubing sets can be assembled to meet the needs of the microbiologist rather than the microbiologist settling for the tubing set-up that is supplied with other closed sterility test systems.

Incubation is carried out in the filter holder itself, thus eliminating the cumbersome task of removing and cutting up the membrane filter – the primary cause of secondary contamination.

The Sartorius sterility testing system is reusable. By simply cleaning the bottles in a dishwasher and autoclaving, the system can be reused as often as needed. The only consumables are the membrane filters. This provides a financial advantage compared to the disposable closed sterility test systems. Moreover, the reusable system produces less waste than do disposables.

Description

The Sartorius sterility testing system consists of a three- to six-branch manifold with the desired quantity of filter holders, a peristaltic pump with inlet needles or tubes, silicone tubing, tee adapter and filling caps with needle for each of the holders. For transfer of the sample and rinsing liquid, a vacuum pump with a suction flask and vacuum tubing is needed.

The main feature of the system is the method of transferring the sample from the original container to the reusable filter holders by means of a peristaltic pump. The tees allow exactly equal volumes of sample from any container to be passed simultaneously into two or three filter holders. Rinsing liquid is pumped into the reusable filter holders in the same way as the culture media, with the latter fed into the different filter holders by alternately closing the individual filling caps. Incubation is carried out directly in the filter holders.

Technical Specifications of the Filter Holders

Material	Filling Bell: Glass Support: Polypropylene Filling Cap: Anodized Aluminum
Gaskets	O-ring & Flat Gasket: Silicone
Filter Diameter	47 mm
Filter Area	12.5 cm ²
Capacity	130 mls
Weight Approx.	120 g
Operating Pressure	Vacuum Only
Sterilization	Autoclave at 121°C

Prevention of Secondary Contamination

The procedure of transferring the sample, the rinsing liquid and the culture media, as well as incubating the culture media in the filter holders, eliminates most of the causes of secondary contamination.

Complete Test Can Be Carried Out in One System

For the first time, sterility testing system allows the complete sterility test to be carried out in one system:

- Transfer of the sample
- Filtration
- Rinsing
- Transfer of the culture media
- Incubation
- Final observation of the growth in the culture media (growth test)

Economical to Use

The system is economical because it is possible to perform the entire test in one system, thus eliminating secondary contamination. The advantageous dimensions of the system with respect to the required volumes of culture media lead to special cost savings. The cost of one test, is only the price of one filter. As a result, the Sartorius sterility testing system is cost-efficient and environmentally friendly.

Variety of Applications

The efficacy of the Sartorius sterility testing system has been proven for testing of ampoule solutions and infusion solutions. In the pharmaceutical industry, it can be used for routine tests and for individual investigations. The method is independent of the sample volume. The entire contents of one infusion bottle can be filtered without interruption.

Ease of Use

The Sartorius sterility testing system can be autoclaved at 121°C with the membrane filter in place. It can easily and rapidly be prepared for use as it is simple to clean and set up. The entire system can be washed in a dishwasher and is detergent-proof.

Variation of Set-ups

The set-up of the system can be varied according to the needs of each individual laboratory; i.e., for one, two or three culture media, for liquid and powder samples. The system is available with a three- or six-branch manifold when two or three culture media are to be used.

EP Sterility Testing

Sartorius Membrane Filters

According to the leading pharmacopeias, membrane filters with a maximum pore size of 0.45 µm are to be used for sterility testing. These filters provide favorable filtration rates even for viscous samples (oils, ointments) and large volume samples (infusion solutions). Various technical publications, however, warn that pseudomonas, for example, is not reliably retained by 0.45 µm membranes and, therefore, 0.2 µm membrane filters should be used. For testing of solutions containing inhibitors (such as preparations containing antibiotics), Sartorius membrane filters with a hydrophobic edge are recommended. These filters enable all growth-inhibiting substances to be rinsed out.

Sterilization

The complete sterility testing system, including the stainless steel manifold, can be autoclaved for 30 minutes at 121°C, 1 bar (~15 psi), prior to the first test. The same manifold is then used for subsequent tests with the previously used filter holders replaced by the sterilized ones (filter holders with membrane filters in place, complete with tubing along with tee and inlet needle). The closing caps must be wrapped separately in aluminum foil prior to autoclaving to avoid secondary contamination.

Culture Media

The USP recommends the use of Fluid Thioglycollate medium and Soybean-Casein Digest medium as culture media. The use of Sabouraud medium has also been recommended in other sources for reliable detection of yeasts and molds as well as aerobic and anaerobic bacteria.

Culture Medium	Incubation temperature
Thioglycollate	30 – 35°C
Soybean-Casein Digest	20 – 25°C
Sabouraud	20 – 25°C

Incubation at least 7 days; maximum efficiency after 2 weeks.

Chemical Resistance of Polypropylene (for continuous use at 20°C)

Weak acids	Resistant
Strong acids	Resistant
Weak alkalis	Resistant
Strong alkalis	Resistant
Alcohols	Resistant
Ethers	Limited resistance
Esters	Limited resistance
Ketones	Limited resistance
Aromatic hydrocarbons	Not resistant
Aliphatic hydrocarbons	Limited resistance
Halogenated hydrocarbons	Not resistant
Oils	Resistant
Propylene glycol	Resistant
Isopropyl myristate	Resistant

Further information about special applications is available on request. Detailed data on the chemical resistance of Sartorius membrane filters is contained in our catalog.

Other Practical Accessories

16612	Vacuum pump (220 V)
16615	Vacuum pump (110 V)
16610	Woulff's bottle
16623	Vacuum tubing (per meter)
16672-1	5 l suction flask
16596 HYK + 01325	Venting unit for sampling

Schematic of the Sartorius Sterility Testing System

1 | Stainless Steel Manifolds 16826 Three-place manifold 16829 Six-place manifold

Two different manifolds are available for supporting the filter holders. A three-place stainless steel manifold is used for a single run with either two or three media. A six-place stainless steel holder is used for either three runs with two media or two runs with three media. The manifolds, which are ideally sized for clean benches (total length 36 cm), feature three-way

valves in each outlet stem for individual control of each filter holder. In addition they have an approx. 10 mm diameter hose nipple for vacuum connection.

2 | Stainless Steel Adapter, 17756

Is attached to each threaded branch on the manifold base.

3 | Silicone Stoppers, 16968

Silicone stoppers have been drilled to accommodate the base of filter holders, allowing the sterile filtration system to be used with Sartorius stainless steel manifolds. These stoppers can also be used to fit into other stainless steel and PVC manifolds.

4 | Filter Holders

Are positioned on the silicone stoppers: 16523 with a 130-ml capacity. These filter holders allow both aerobic and anaerobic incubation, are easy to clean, dishwasher safe and resistant to autoclaving at 121°C.

Glass|Polypropylene Filter Holder, 47 mm, 130 ml, 16523

Has a graduated mark at the 60-mm level (56-ml capacity) and at the 115-mm level (110-ml capacity).

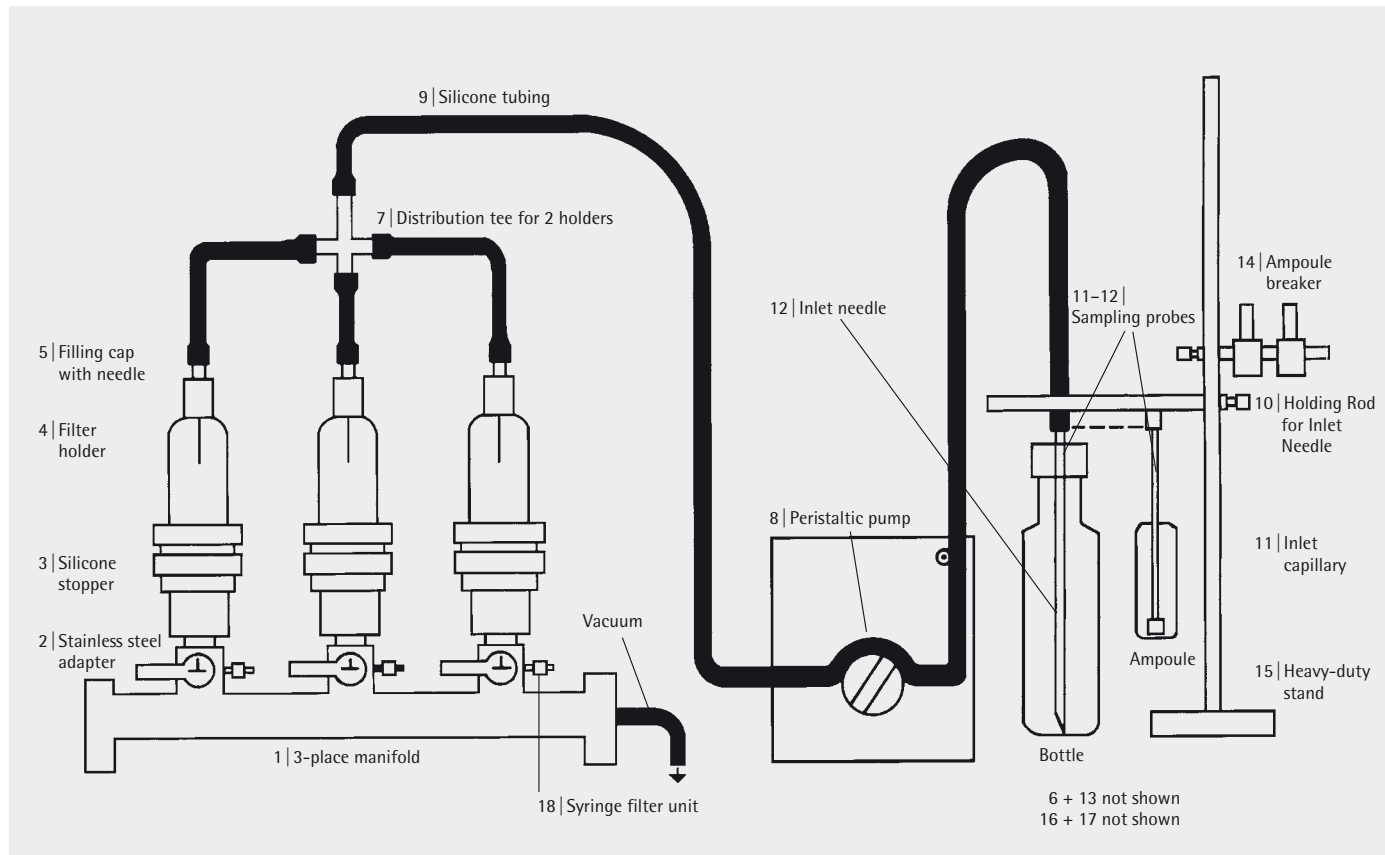
5 | Filling Cap with Needle, 16967

These special anodized aluminum feed-through caps feature a needle probe that extends 50 mm down into each bell. This allows accurate filling of each holder to the minimum level for media. After filling, these feed-through caps are removed and replaced with solid caps for incubation. The feed-through caps have a hose barb for 4 + 1.6 mm tubing.

6 | Tube Clamps, 16978 (Package of 6)

For clamping off tubing between the distribution "T" or "X" adapter and cap while culture medium is filled in a filter holder that is not clamped off. Not autoclavable.

Schematic of the Sartorius Sterility Testing System



7 | Distribution Adapters

Two types are available:
16965 for 3 filter holders (X adapter)
16966 for 2 filter holders (T adapter)
 Stainless steel inserts with a 1-mm drill hole in the outlet barbs of these plastic adapters ensure practically equal distribution of liquid into the 2 or 3 filter holders. Outer diameters of the hose barbs: 5.5 mm.

8 | Peristaltic Pump, 16696

The peristaltic pump features variable speed and reversible control for easy and precise transport of solution through the silicone tubing (4 × 1.6 mm). For 110 V and 220 V.

9 | Silicon Tubing, 16699

10-m tubing, 4 × 1.6 mm, for connecting the inlet tube or needle to the distribution adapter and this adapter to the filling caps with needles. Sterility testing of infusion bottles subjects the tubing to greater stress than that during testing of ampoules; therefore, the tubing must be exchanged more frequently.

10 | Holding Rod for Inlet Needle, 16974, with Clamp Holder

Stainless steel holding rod with spring closure.

11 | Stainless Steel Inlet Tube for Ampoules, 16963

With screen on the suction side to stop glass fragments from entering the tubing. Length 20 cm. Outlet hose nipple with 5-mm diameter.

12 | Stainless Steel Inlet Needle for Infusion Bottles, 16964

Needle-shaped to pierce the rubber septa or caps of infusion bottles. The entry hole for the sample is on the side to prevent blockage by rubber particles that may be released as the septum is pierced. Outlet hose nipple with 5-mm diameter.

13 | Clamp Holder, 16976

Clamp holders are required to attach the ampoule breaker and the peristaltic pump to the Sartorius stand.

14 | Ampoule Breaker, 16969

The ampoule breaker features two blocks, one for small and one for large ampoules. The scored ampoule is simply inserted in the breaker and snapped open. The tongs firmly hold the ampoule and enable the operator to safely open the ampoules.

15 | Heavy-Duty Stand, 16970

A heavy-duty stand, or rod system, must be available to hold the probe, ampoule breaker, etc.

16 | Incubation Rack, 16975

Accommodates up to 12 filters holders and prevents messes in the incubator if any culture media leakage occurs.

17 | Ampoule Holding Tongs, 16973

The holding surfaces have a special elastic silicone coating to allow simple handling of ampoules without the danger of breakage.

18 | Syringe Filter Units, 15 mm, 17574 K (box of 50)

Are attached to the side holes of the manifold taps to ensure sterile vacuum release.

Selecting the Complete Equipment Required

The particular choice of components depends on the type of sample (ampoules or infusion solutions in bottles), the number of batches to be tested per day, and the number of culture media to be used. The minimum equipment configuration to be ordered is yielded by the following:

A Number of system parts that are to be used in incubation:

Incubation time × number of media/batch × batches/day

B Number of system parts that are to be cleaned after every batch:

Batches/day × 2

C Number of system parts that are to be cleaned at the end of the day:

Number of media/batch

D Number of articles of consumption per year:

Number of media/batch × batch/day × workdays/year

Please remember to calculate the quantity needed as reserve stock (positive controls, replacement parts, etc.)

The following tables list examples of the recommended equipment needed for approximately one year, assuming a 14-day incubation period and appropriate reserve stock for 2–3 days.

Number of batches to be tested per day		1		2		3		5		10	
Number of culture media to be used		2	3	2	3	2	3	2	3	2	3
A	16522 23 Filter holder	20	30	40	60	60	90	100	150	200	300
	16826 Manifold	1	1	1	1	1	1	1	1	1	1
C	17756 Stainless steel adapter	2	3	2	3	2	3	2	3	2	3
B	16965 X-distributor	–	1	–	2	–	3	–	5	–	10
B	16966 T-distributor	1	–	2	–	3	–	5	–	10	–
B	16967 Filling cap with filling needle	2	3	4	6	6	9	10	15	20	30
C	16968 Silicone stoppers	2	3	2	3	2	3	2	3	2	3
	16696 Peristaltic pump	1	1	1	1	1	1	1	1	1	1
B ÷ 10	16699 Silicone tubing, 10 mm	1	1	1	1	1	2	2	2	3	4
	16974 Holding rod ¹⁾ ²⁾ for inlet tube needle	1	1	1	1	1	1	1	1	1	1
A ÷ 12	16975 Incubation rack	2	3	4	5	5	8	9	13	17	25
	16978 Tube clamps (tubing clips)	1	1	1	1	1	1	1	1	1	1
C	17574 K Venting filters, 50	2	3	2	3	2	3	2	3	2	3
D	3) Membrane filter, 47 mm, 100	5	8	10	15	15	23	25	38	50	75

¹⁾ for ampoule testing ²⁾ option of emptying the infusion bottle upside down ³⁾ membrane filters for sterility testing (see below)

Additional equipment:

Number of batches to be tested per day		1		2		3		5		10	
Number of culture media to be used		2	3	2	3	2	3	2	3	2	3
a) For ampoule testing											
B	16963 Inlet tube	1	1	2	2	3	3	5	5	10	10
	16973 Ampoule holding tongs	1	1	1	1	1	1	1	1	1	1
	16969 Ampoule breaker	1	1	1	1	1	1	1	1	1	1
	16976 Clamp holder	2	2	2	2	2	2	2	2	2	2
	16970 Support stand ²⁾	1	1	1	1	1	1	1	1	1	1
b) For testing infusion solution in bottles											
B	16964 Inlet needle (long)	1	1	2	2	3	3	5	5	10	10
B	16964-3 Inlet needle (short) ²⁾	1	1	2	2	3	3	5	5	10	10

Normally, cellulose nitrate membrane filters are used in sterility testing. Edge-hydrophobic membrane filters are recommended for sterility testing of samples containing inhibitors, such as antibiotics.

Type of membrane filter	Pore size 0.45 µm	Pore size 0.2 µm	Application
Cellulose nitrate (CN)	11306-047 N	11407-047 N	pH 4–8 most hydrocarbons
CN with hydrophobic edge	13106-047 HCN	13107-047 HCN	
Cellulose acetate (CA)	11106-047 N	11107-047 N	pH 4–8, most alcohols, hydrocarbons and oils
CA with hydrophobic edge	13506-047 HCN	13507-047 N	
Regenerated cellulose	18406-047 N	18407-047 N	pH 3–12, solvent-resistant

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