User Guide

mdi Stericheck – LVP

for Large Volume Parenterals : Glass Bottles

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1. Introduction

Sterility testing is critical to quality control of sterile pharmaceutical product manufacture and has become all the more important because of the regulatory and commercial considerations. International pharmacopoeias recommend use of procedures that ensure elimination of secondary contamination for accurate and reproducible results.

As per USP "Pharmacopeial articles are to be tested by the Membrane Filtration method where the nature of the product permits". The membrane filtration method involves filtration of samples drawn from an aseptically manufactured product lot through the membrane filter followed by washing away of any growth inhibiting substances, cutting the membrane filter into two equal halves and incubating these in nutrient media suitable for growth of aerobic and anaerobic microorganisms.

The sterility of the lot under test is confirmed only if no growth is observed after the specified number of days of incubation. The USP also states that the presence or absence of microbial growth observed as turbidity should not be due to any external contamination (false positives) or presence of any inhibitory substances (false negatives).

Such situations that compromise the reliability of the test is a serious issue as retesting has very limited scope and frequent investigations and revalidations is a highly undesirable activity.

Therefore it is very important for the microbiologist to ensure that no external contaminants are introduced during the sterility test procedure and that it meets all the other pharmacopoeia needs.

This guide describes the procedure to use of **mdi Stericheck** – LVP, the closed sterility-testing device for large volume parenterals in glass bottles.

2. Closed Sterility Testing Device

Stericheck: Closed Sterility Test System

mdi Stericheck Closed Sterility Test System offers the complete sterility testing solution. Right from sampling, filtration, media exposure, until incubation, the entire activity takes place in a closed loop to do away with the possibility of any extraneous contamination and therefore false positives. The absence of anti-microbial/ bacteriostatic components, and complete washing away such substances in the drug product ensures no false negatives.

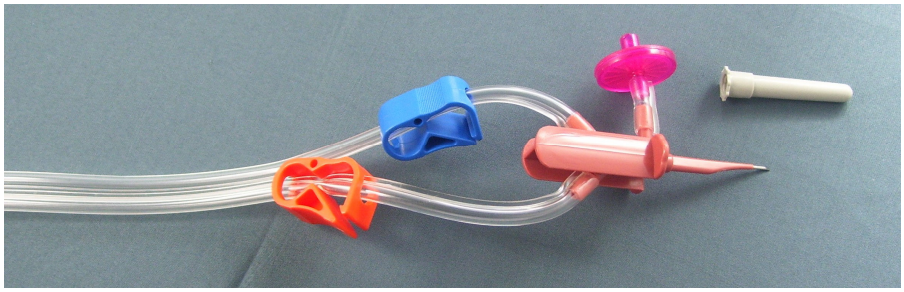
Advantages

* Fast
* Pre- sterilized and ready to use
* No membrane handling
* No false positives or negatives

The Stericheck system incorporates disposable Stericheck devices and a specially designed easy to use Steripump for aseptic transfer of fluids.

Specifications

Material of Construction of Stericheck LVP	
Membrane	Cellulose Nitrate/ Nylon-66/PVDF
Membrane Pore Size	0.45µm
Canisters	SAN (Styrene Acrylo Nitrile), plain transparent
Tubing	PVC, plain transparent
Needle	Stainless Steel
Filter on Vented Needle	0.2 µm PTFE Membrane
Filter on Canister Vent	0.2 µm PTFE Membrane
Canister Dimension	51 mm (Diameter) x 120 mm (Height)
Water Flow Rate	> 0.3 lpm @ 10 psi at 25°C
Sterilization	ETO Sterilized
Maximum Operating Temperature	45°C continuous
Maximum Operating Pressure	45 psi



Pic. 1: Tubing with Needles and Vent Filter for LVP

3. Procedure of Use

3.1 Using **Stericheck** LVP: The set-up requirements and steps to be sequentially followed for using LVP Canisters are as below.

Requirements:

a. **mdi** Steripump

b. **Stericheck** LVP Canister pack, presterilized

c. Product to be tested

d. Incubators

e. Sterile Fluid Thioglycollate (FTG) Medium – 100 ml.

f. Sterile Soybean Casein Digest (SCD) Medium – 100 ml.

g. Indian/US/European pharmacopoeia

h. Aseptic laboratory environment

i. Rinse solution as recommended in referred pharmacopoeia – USP/EP/IP/Other

Steps

A. Set up the Steripump

B. Position the canisters and the tubing on the pump

C. Prewet the membranes

D. Prepare the product samples to be tested

E. Test the product

F. Rinse the tubing, canisters, and membranes

G. Add media to the canisters

H. Incubate the canisters

A. Set up the Steripump:

Set up the peristaltic pump. Please refer to Steripump User Manual for more details.

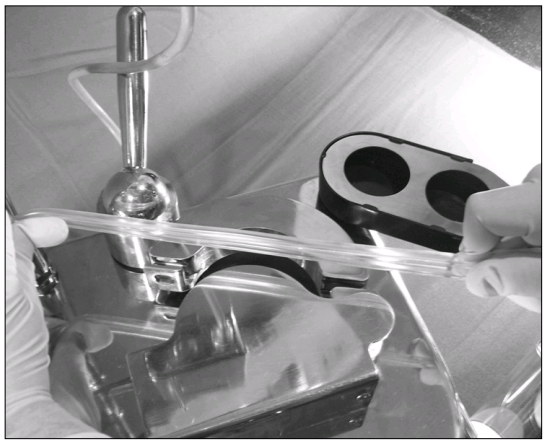
Pic.2: mdi Steripump Unit

B. Position the Canisters and Tubing on the Pump:

- Open the sterilized plastic tray that contains the Stericheck canisters and tubing-needle set by peeling back the lid in an aseptic environment.
- Remove the canisters and tubing-needle set from the plastic tray.
- Place the canisters upright into the canister openings of the drain tray.

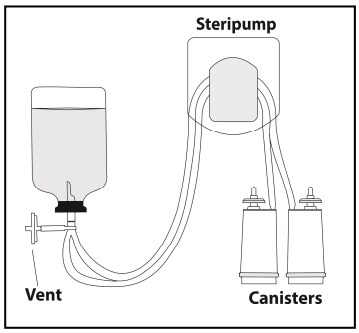
Pic. 3: Stericheck canisters placed on the drain tray

- Load the canister tubing into the pump head. Refer installation.



Pic. 4: Placement of PVC tubing in the Steripump head

- Open the pouch that contains the caps and plugs and place them inside the blister package or on a surface free of contamination.



Pic. 5: Schematic Set-up of Stericheck LVP

C. Prewet the Membranes:

Reference Document:

Please refer to the following

- United States Pharmacopoeia (USP)/ European Pharmacopoeia (EP)/ any other international pharmacopeia for information on the rinse solution you should use for your application.
- **mdi** Steripump User Manual for operating the peristaltic pump

Important:

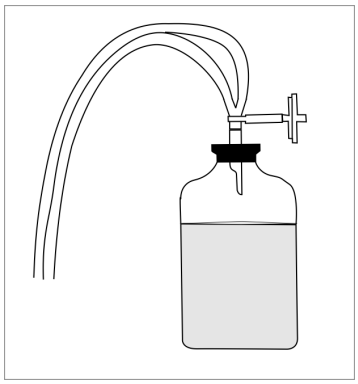
- Remove the red caps from the air vents on top of the canisters to fill the canisters.
- Replace the red caps on the top air vents while emptying the canisters.

Procedure to prewet the membranes:

I. Decontaminate the surfaces of the rinse container carefully, particularly the top septum area that is to be pierced later in this process.

II. Remove the protective cap from the Stericheck product-testing needle.

III. Insert aseptically the Stericheck needle into the rinse container while holding the container upright.



Pic. 6: Indicative position of rinse container

Important:

- *If using a flame, swiftly flame the needle, allow it to cool and then insert into the rinse container.*
- *Insert the needle up to its base to ensure the needle opening is inside the container.*

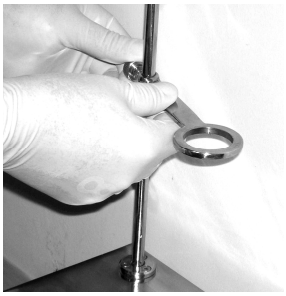
IV. Switch on the Steripump, and adjust pump at the appropriate speed.

Caution:

- *The pump speed should be kept at moderate level as higher speed may allow the fluid to splash up and wet the canister vent. This may cause water logging of the canister vent membrane and prevent the canister from filling. Although special flow directors inside the* **mdi** *Stericheck canisters minimize the chances of this happening.*

V. Turn on the pump. (Alternatively, if using the foot control accessory, press the pedal down with foot to keep the pump running.)

VI. Invert the rinse container and place it in the bottle support system.

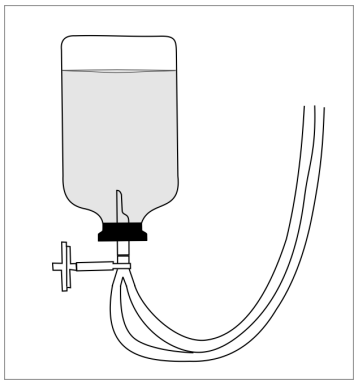


Bottle Holder Bar

Stabilizing Bar

Bottle Insertion

Pic. 7: Bottle Support System



Pic. 8: Indicative position of rinse container

VII. Transfer the sterile rinse solution (approximately 25 ml) to pass on into each Stericheck canister.

VIII. Aseptically place a red cap onto the top of each canister's air vent to allow the rinse solution to start filtering through the membranes.

IX. Take off rinse solution container from the bottle support assembly and keep it upright on your work surface.

X. Take off the red caps from the top of each canister when approximately 1 cm (0.39 in) of liquid remains in each canister.

Important:

- **mdi** *recommends to leave a small amount of fluid on the membrane at the base of canister to ensure that the test product is suspended in rinse solution before filtration.*

XI. Turn off the pump. (If using the foot control accessory, lift your foot off the pedal to turn off the pump.)

D. Prepare the Product Samples to be Tested:

I. Decontaminate the surfaces of each product container carefully, particularly the top septum area that is to be pierced later in this process.

II. Remove Stericheck needle from the rinse container.

Important:

- *If you are using a flame, quickly flame the needle and allow it to cool.*

III. Hold upright the first container of the product to be tested. Aseptically insert the needle up to the needle's base to ensure that the needle opening is inside the container.

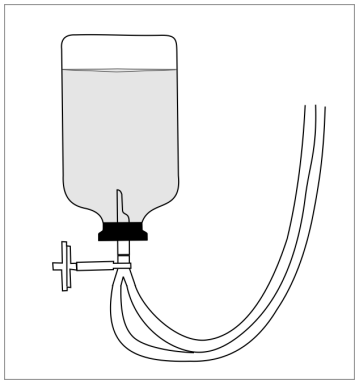
E. Test the Product:

I. Turn on the pump. (Alternatively, if using the foot control accessory, press the pedal down with foot to keep the pump running.)

Caution:

- *The pump speed should be kept at moderate level as higher speed may allow the fluid to splash up and wet the canister vent. This may cause water logging of the canister vent membrane and prevent the canister from filling.*

II. Invert the first product container and place it in the bottle support setting with the help of stabilizing bar.



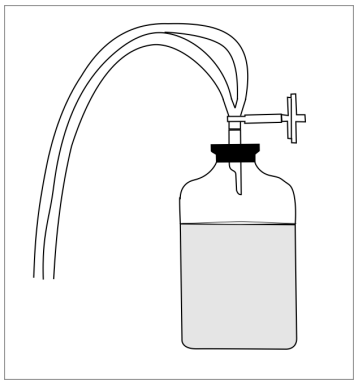
Pic. 9: Indicative position of product container

III. Aseptically place a red cap onto the top of each canister's air vent.

IV. Transfer the entire contents (or the volume recommended by USP, EP, or international pharmacopoeia) of this container to the canisters.

V. Turn off the pump. (If using the foot control accessory, lift the foot off the pedal to turn off the pump.)

VI. Remove the container from the support assembly and place it upright on the work surface. Place the second container to be tested next to the first. Decontaminate the second container before testing as earlier.



Pic. 10: Indicative position of product container

VII. Remove the Stericheck needle from the first container and aseptically insert it into the second container.

Important:

- *If you are using a flame, quickly flame the needle and allow it to cool before inserting it into the next container.*

VIII. Turn on the pump. (If you are using the foot control accessory, press your foot down on the pedal to turn on the pump.) The pump will return to its preset speed.

IX. Invert the second container and place it into the support, and transfer the product as before.

X. Repeat the earlier steps until the last sample in the lot is transferred and filtered.

XI. Remove the product container from the bottle support assembly and keep it upright on work surface. Then turn on the pump.

XII. Continue pumping until all residual product clears the tubing and filters through the canisters. Then turn off the pump.

Important:

- *In order to preserve the sterility of the closed system, keep the needle in the product container until you are ready to transfer it to the rinse fluid container.*

F. Rinse the Tubing, Canisters, and Membranes:

Reference Document:

Please refer to the following

- United States Pharmacopoeia (USP)/ European Pharmacopoeia (EP)/ any other international pharmacopeia for information on the rinse solution to be used for your application.
- The volume of rinse solution is predetermined during the validation procedure.

Procedure:

I. Remove the red caps from the air vents on top of the canisters.

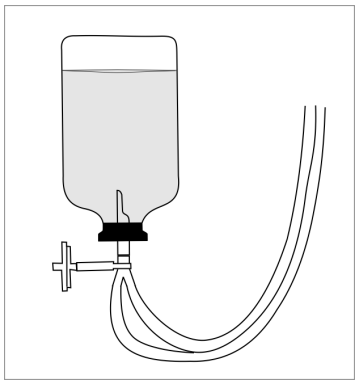
II. Take out the Stericheck needle from the product container and insert it up to its base into the rinse solution bottle.

Important:

- *If using a flame, swiftly flame the needle and cool it and then insert into the rinse solution bottle.*

III. Set the pump speed at 55 or lower and turn on the pump. (If using the foot control accessory, press the pedal with foot to keep the pump running.)

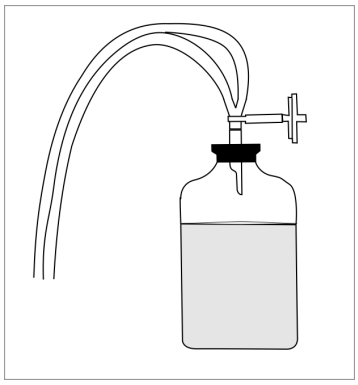
IV. Invert the rinse bottle and place it into the bottle support system.



Pic. 11: Indicative position of rinse container

V. Pump 100 ml of rinse solution into each canister. Now turn off the pump.

VI. Remove the rinse solution bottle from the bottle support system and place it upright on your work surface.



Pic. 12: Indicative position of rinse container

VII. Aseptically replace the red caps onto the top air vents of the canisters. Keep the needle in the bottle.

VIII. Turn on the pump and allow the rinse fluid to filter slowly through the canisters until the canisters are empty. Then turn off the pump.

IX. Repeat the above steps continue rinsing (100 ml of rinse solution per canister, at a time) according to your validated standard operating procedure until the appropriate volume of rinse solution filters through the canisters, tubing, and membranes.

Caution:

- *The needle from the rinse solution bottle should not be removed in order to preserve closed system sterility. If needle is taken out, the contaminated air may enter the tubing and canisters.*

G. Add Media to Canister

Sterile Fluid Thioglycollate (FTG) media and sterile Soybean Casein Digest (SCD) media in separate 100ml bottles with rubber septum caps are to be prepared and kept ready for transfer to the canisters.

Special pre-installed color coded clamps on the canister tubing will help avoid mixing of the two different media types in the canisters during transfer.

I. Remove the red caps from the air vents of the canisters.

II. Lift one of the canisters from the drain tray. Aseptically place a red plug into the bottom outlet port of the canister. Place the canister again in the drain tray and repeat the procedure for the other canister.

Important:

Secure the red plug firmly by twisting a half turn while pushing it into place on the bottom outlet port of the canister.

III. Clamp off one tubing line by closing the blue clamps (pre-installed). Place this clamp as close as possible to the Y-connector of the needle- spiking device.

IV. Clean and decontaminate the FTG media bottle septum. Insert the Stericheck needle into the FTG media bottle.

Important:

- *If you are using a flame, quickly flame the needle and allow it to cool before inserting it into the media bottle.*

V. Turn on the pump. Then invert the media bottle and place it in the bottle support system. Transfer the media into one canister.

Caution:

- *Keep the pump speed at 35 - 40 when pumping Fluid Thioglycollate Medium to reduce aeration.*

VI. Turn off the pump when the tubing is clear of media.

VII. Remove the FTG media bottle from the bottle support and set it upright on your work surface.

VIII. Open the blue clamp from the tubing. Clamp (red clamp) the other tubing line (where media has just been transferred through) as before.

IX. Remove the Stericheck needle from the FTG media bottle and insert it into the SCD media bottle.

Important:

- *If you are using a flame, quickly flame the needle and allow it to cool before inserting it into the second media bottle.*

X. Turn pump on, invert the media bottle, and place it in the bottle support system.

XI. Transfer the media from second bottle into the second canister. Then turn off the pump when the line is clear of media. Remove the media container from the bottle support and place it upright on your work surface.

Caution:

- *To preserve the sterility of the closed system, do not remove the needle from the last media bottle, as this can potentially allow contaminated air to enter the tubing and canisters.*

H. Incubate the Canisters

I. Clamp off both tubing lines approximately 6 cm from the canister inlets.

II. Remove the tubing from the pump.

Caution:

- *To preserve the sterility of the closed system, do not remove the needle with the tubing from the last media bottle. This could allow contaminated air to enter the tubing and canisters.*

III. Now cut the tubing approximately 2 cm above the clamps with sterile scissors, so that the canisters remain closed to the environment.

IV. Fold over and insert the tubing onto the air vents on top of the canisters.

V. Remove the canisters from the drain tray and incubate for time and temperature as recommended by the pharmacopoeia being followed.

VI. Observe for the presence or absence of turbidity to indicate the presence or absence of microorganisms.