Sterile Filtration of Product Using 0.2 Micron Filtration Unit

SOP 15101 **Rev. 06**

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1.0 Purpose

This procedure describes the use of 0.2 micron filters for sterile filtration of liquids.

2.0 Scope

This procedure applies to Biopharmaceutical Development Program (BDP) personnel performing sterile filtration using 0.2 micron filters. These procedures will also be used when performing final product filtration using 0.45 Micron filters.

3.0 Authority and Responsibility

3.1 The Manager of Technical Operations, Biopharmaceutical Development Program (BDP) has the authority to define this procedure.

3.2 Area managers, Technical Operations, BDP, are responsible for training laboratory personnel in this procedure and for documenting this training to Biopharmaceutical Quality Assurance (BQA).

3.3 BDP personnel are responsible for the implementation of this procedure.

3.4 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this operation.

4.0 Equipment and Materials

4.1 0.2 micron hydrophilic filter (size and type vary according to the properties and quantity of the material to be filtered).

4.2 Certified Biological Safety Cabinet (BSC) or class 100 Laminar Flow workstation.

4.3 Appropriate lab attire. Sterile gloves and sleeves will apply to work in a BSC in addition to the normal gowning requirements.

4.4 Silicone tubing as required.

4.5 Various tubing connectors as required.

4.6 70% isopropyl alcohol (BDP PN 30129).

4.7 Vacuum source, peristaltic pump, syringe or pressure vessel.

4.8 Pressure gauge as required.

5.0 Procedure

5.1 General Process Requirements

5.1.1 Disinfect the BSC or Class 100 workstation before use as per **SOP 19102 - *Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers and Centrifuges***.

5.1.2 Operators must practice good aseptic technique while performing the following procedures.

5.1.3 Remove all materials and equipment from the hood that is not to be used in the filtering process.

5.1.4 Disinfect the outer surfaces of all items being placed into the BSC or Class 100 workstation with 70% sterile isopropyl alcohol (IPA).

5.2 Bottle-Top Filtration Using Vacuum Pressure

5.2.1 Screw the bottle-Top filter onto a pre-sterilized bottle. Sterile filters may be provided as an assembled unit with the bottle already attached.

5.2.2 Connect the filter unit to the vacuum source.

5.2.3 Pour the product into the top chamber of the filter unit.

5.2.4 Turn on the vacuum source.

5.2.5 Continue to add product during the process.

5.2.6 When the top chamber is empty, disconnect the vacuum source from the filter unit.

5.2.7 Carefully unscrew the filter from the bottle.

5.2.8 Place a sterile cap onto the bottle and tighten.

5.3 Sterile Filtration Using a Capsule Filter and Positive Pressure

5.3.1 All tubing and connectors on the downstream (outlet) side of the filter must be pre-sterilized.

5.3.2 Connect a section of tubing to the upstream (inlet) side of the filter.

5.3.3 Insert the above tubing section into a peristaltic pump and connect to the container of material to be filtered.

NOTE: A pressure vessel can be substituted for the peristaltic pump as a suitable alternative for providing positive pressure to push material through a filter. In this case, compressed gas would be run through a regulator to control the amount of pressure on the system.

5.3.4 If filling into a bag:

5.3.4.1 Attach a section of pre-sterilized tubing to the outlet of the filter. Secure with a cable tie.

5.3.4.2 Attach the other end of the sterile tubing using an appropriate connecter to a sterile bag.

5.3.4.3 Turn on the pump slowly. Observe carefully to ensure that the product is being drawn out of the feed vessel towards the filter.

5.3.4.4 Open the bleed valve to release any air trapped in the filter.

5.3.4.5 Once all of the air is out of the filter, close the bleed valve. Monitor the pressure in the system to ensure that the tubing does not swell. This may be accomplished by inserting a pressure gauge between the pump and filter or by simply feeling the tubing between the pump and filter and noting any excessive pressure on the walls of the tubing.

5.3.4.6 Pressure on the system can be reduced, if necessary, by reducing the pump speed. If the pressure continues to build beyond acceptable limits, the filter may be clogging. Consult the Area Supervisor if this occurs.

5.3.4.7 A higher flow rate of material through the filter can be achieved by increasing the pump speed if pressure build-up and/or flux rate is not prohibitive.

5.3.4.8 Once all the material has been filtered or the bag is full, turn off the pump. Using a pair of hemostats, clamp off the tubing between the filter and the bag.

5.3.4.9 Drain any residual material left in the tubing into the bag. Close the pinch clamp on the bag.

5.3.4.10 Disconnect the tubing from the bag. Place a sterile plug/cap of appropriate size on the bag to seal it. Repeat the process by connecting additional bags as necessary.

5.3.5 If filling into a bottle:

5.3.5.1 There should be a filling bell attached to the filter outlet. Place the filter in a clamp to hold it just above the neck of the bottle. The bleed valve must be slightly higher than the rest of filter. Place the bottle under the filling bell.

5.3.5.2 Turn on the pump slowly. Open the bleed valve to release air pressure from the filter. Be careful not to allow any product to escape from the bleed valve and drip on the filling bell, as this material will be non-sterile. Close the bleed valve.

5.3.5.3 Adjust the speed of the pump for the best flow rate (see Sections 5.3.4.6 and 5.3.4.7). Keep splashing to a minimum. Turn off the pump once the bottle is filled to the correct volume. Place a cap on the bottle. Place the next bottle under the filling bell in the same manner.

5.3.5.4 Repeat the process until all product has been sterile filtered.

5.4 Sterile Filtration Using a Syringe Filter with Positive Pressure

5.4.1 All tubing and connectors on the downstream (outlet) side of the filter must be pre-sterilized.

5.4.2 If filling into a bag:

5.4.2.1 Transfer product into the syringe and connect syringe to the syringe filter.

5.4.2.2 Attach a section of pre-sterilized tubing to the outlet of the filter. Secure with a cable tie.

5.4.2.3 Attach the other end of the sterile tubing using an appropriate connecter to a sterile bag.

5.4.2.4 Apply pressure to the syringe plunger.

5.4.2.5 Maintain a steady pressure on the plunger. Observe the flow rate of product into the bag. If the flow rate decreases, slightly increase pressure on the plunger. If flow rate continues to decrease, maintain current pressure on the plunger, until filtration is completed or stop filtration and replace filter.

CAUTION: Very high pressures can be generated using a syringe. Do not attempt to increase pressure on plunger to get the last amount of liquid through the filter.

5.4.2.6 Once all the material has been filtered or the bag is full, release pressure on the syringe. Using a pair of hemostats, clamp off the tubing between the filter and the bag.

5.4.2.7 Drain any residual material left in the tubing into the bag. Close the pinch clamp on the bag.

5.4.2.8 Disconnect the tubing from the bag. Place a sterile plug/cap of appropriate size on the bag to seal it.

5.4.3 If filling a bottle

5.4.3.1 Transfer product into the syringe and connect syringe to the syringe filter.

5.4.3.2 Attach a section of pre-sterilized tubing to the outlet of the filter. Secure with a cable tie.

5.4.3.3 Attach the other end of the sterile tubing using an appropriate connecter to a sterile bottle.

5.4.3.4 Apply pressure to the syringe plunger to obtain a steady flow.

5.4.3.5 Observe the flow rate of product into the bottle. If the flow rate decreases, slightly increase pressure on the plunger. If flow rate continues to decrease, maintain current pressure on the plunger, until filtration is completed or stop filtration and replace filter

CAUTION: Very high pressures can be generated using a syringe. If the filter is plugged do not increase pressure on the plunger to force more liquid through the filter.

5.4.3.6 Once all the material has been filtered or the bottle is full, release pressure on the syringe.

5.4.3.7 Drain any residual material left in the tubing into the bottle. Clamp the tubing between the connection and the bottle.

5.4.3.8 Disconnect the syringe from the tubing. Place a sterile plug/cap of appropriate size into the connector on the tubing.

5.5 Post-use integrity testing must be performed on all integrity testable filters as per **SOP 15114 - *Bubble Point Test for 0.2 Micron Filters*** or **SOP 12240 - *Testing Filters with the Sartocheck 5 Integrity Test System***.

6.0 Documentation

6.1 Document in the appropriate Batch Production Record (BPR) the filter part number, lot number (both BDP and Manufacturing), expiration date, and the results of the bubble point test.

7.0 References and Related Documents

SOP 12240 Testing Filters with the Sartocheck 5 Integrity Test System

SOP 15114 Bubble Point Test for 0.2 Micron Filters

SOP 19102 Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers and, Centrifuges

8.0 Change Summary