# Large Volume Parenteral and Small Volume Parenteral Filtration

*Enables more rigorous process control to improve sterile drug quality*

## INTRODUCTION

Large volume parenteral (LVP) and small volume parenteral (SVP) are sterile injectable drugs. There are two broadly used methods to produce a sterile drug product: terminal sterilization and aseptic processing of sterilized unit component. For terminal sterilization, in most cases, the product, container, and closure have low bioburden but are not sterile at the time of filling. The product is subjected to a sterilization process in its final container. With aseptic processing, the product is at higher risk of microbial contamination than with terminal sterilization. In an aseptic filling process, the product, containers, and closure are sterilized separately and then brought together under an extremely high-quality environmental condition. It is a well-accepted principle that sterile drugs should be manufactured using aseptic processing only when terminal sterilization is not feasible.

LVPs are sterile drugs packaged in containers labeled as containing more than 100 mL. Most are terminally sterilized, but some can be sterilized by filtration and aseptically processed. SVPs are sterile drugs packaged in containers labeled as containing less than 100 mL. They can be classified into different types including prefilled syringes, ampules, or lyophilized powders. Many SVPs are heat labile requiring sterilizing filtration and aseptic processing.

## TYPICAL LVP/SVP PRODUCTION PROCESS

To minimize risks of microbial, particulate, and pyrogen contamination, sterile product manufacturing requires special processes. Sterilizing filtration is a critical part of any aseptic process, which is removing microorganisms from a fluid stream without adversely affecting product quality. Typical applications include liquid and air/gas sterile filtration.

Multiple factors will affect the effectiveness of any sterilizing filtration process, including the type and number of microorganisms, the properties of the liquid, the filter design and membrane polymer, and the filtration process parameters.

For terminally sterilized products, the bulk solution process should include a filtration step with a microorganism reduction filter or sterilizing grade filter to control bioburden levels and particulates prior to filling final product containers, Figure 1.

If the product cannot be sterilized in the final container, solutions or liquids should be sterilized by filtration through a sterilizing grade filter. Due to the potential additional risks of a sterile filtration process, as compared with other sterilization processes, a second filtration through a sterile sterilizing-grade filter should be taken into consideration, which is also called redundant filtration, Figure 2.

Large Volume Parenteral

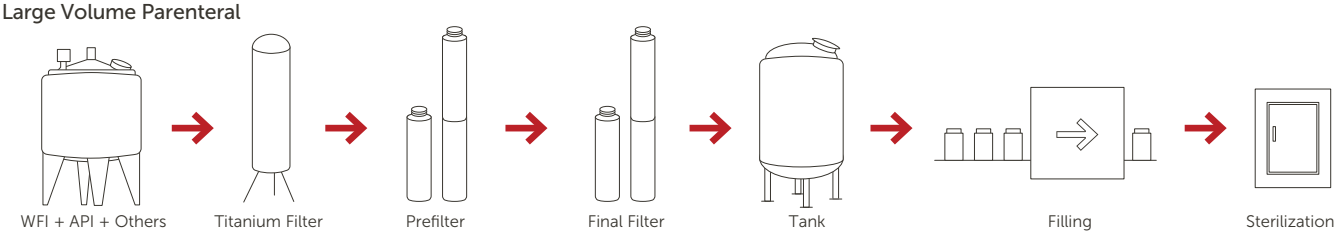


*Figure 1. Typical LVP manufacturing process.*

Small Volume Parenteral

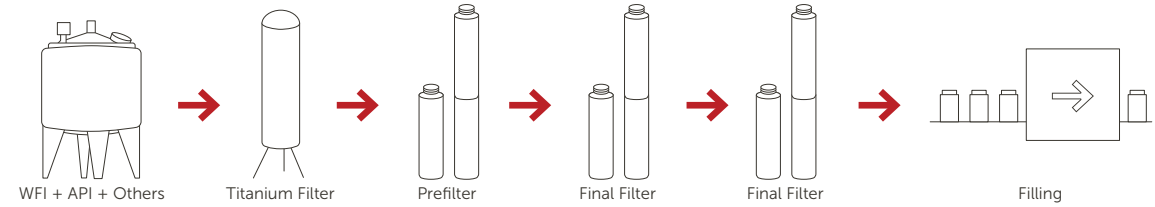


*Figure 2. Typical SVP manufacturing process.*

## SEPARATION GOALS

- Prefiltration – removes the colloids and particles contaminants, extends the service life of down-stream sterilizing filters.
- Final filtration – sterilizing filtration is a process that can be validated to consistently yield filtrates that are sterile. This is best accomplished by using filters with very low active pharmaceutical ingredient (API) binding, low extractables, and nonpyrogenic. In addition, sterilizing filters must be integrity-tested and either readily sterilizing or supplied presterilized.

## REGULATORY COMPLIANCE

1. Filters with silicone O-rings or gaskets meet the requirement of USP <88> Plastic Class VI
2. All components meet the FDA Indirect Food Additive requirements cited in 21 CFR 177-182
3. All components meet the (EC) No 1935/2004
4. Manufactured in accordance with an ISO 9001 and ISO 13485 certified quality management systems
5. Meet the particle requirement for SVP set by USP and China Pharmacopeia

## LVP/SVP FILTRATION RECOMMENDATIONS

As your trusted partner, Entegris is dedicated to ensuring you have peace of mind throughout every step of your processes. We have filtration expertise and technologies for every filtration step during LVP/SVP production. Our portfolio will help improve sterile drug quality and optimize your production experience.

| Application | Recommendation |
|---|---|
| Prefiltration | Pharmsteri™ PP cartridge series<br>Pharmsteri PES cartridge series |
| Bioburden reduction | Pharmsteri PES cartridge series |
| Final sterile filtration | Pharmsteri PES cartridge series |
| Venting sterile | Pharmsteri PTFE cartridge |

*For detailed product information contact Entegris.*

*Pharmsteri PES/PP cartridge filters.*

## APPLICATION SUCCESSES

Entegris had helped numerous customers apply filtration to their formulation processes, and enabled them to successfully remove contamination risks and maintain more rigorous process control. To gain peace of mind in your process, contact Entegris.

### FOR MORE INFORMATION

Please call your Regional Customer Service Center today to learn what Entegris can do for you. Visit entegris.com and select the Contact Us link to find the customer service center nearest you.

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