



# Valve Selection for Sterilizers in cGMP Applications



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### Abstract

Ensuring uncompromising sterility in cGMP (Current Good Manufacturing Practice) environments requires safe sterilization equipment. While diaphragm valves have traditionally been perceived as the industry standard for aseptic design, the extreme mechanical and thermal stresses of high-frequency steam sterilization often expose their vulnerabilities.

This white paper examines the operational contrast between traditional diaphragm valves and modern piston valves. It addresses common misconceptions regarding sterile boundaries and bioburden management while demonstrating how piston valves provide more robust mechanical resilience, precise steam modulation, and can contribute to a lower total cost of ownership over the valve lifecycle.



# Introduction

In cGMP (Current Good Manufacturing Practice) environments, effective sterilization is paramount to maintaining both safety and regulatory compliance. Every component within these systems must perform under extreme conditions without compromising sterility. While diaphragm valves have traditionally been the industry standard, evolving demands for increased uptime and tighter process control have highlighted their limitations. This white paper explores the technical and operational advantages of piston valves, demonstrating how they provide more robust durability, cleanability, and a lower total cost of ownership in modern pharmaceutical and biotech sterilization processes.

# Standards Expected in cGMP Sterilizers

A sterilizer is classified as cGMP when its design and operation are validated to ensure a Sterility Assurance Level (SAL) of  $10^{-6}$ .<sup>1</sup> To achieve this, every square centimeter of the chamber and its associated piping must be sterilized by clean steam. The valves in these systems act as the primary control points of the sterile boundary; they must handle rapid vacuum pulses, withstand repeated exposure to high-pressure steam (often up to approximately 9 bar), and operate across wide temperatures (often from  $-40^{\circ}\text{C}$  to  $+210^{\circ}\text{C}$ ). Performance characteristics depend on proper valve selection and specification within validated operating ranges, which for Getinge systems typically include temperatures from approximately  $-10^{\circ}\text{C}$  to  $+180^{\circ}\text{C}$  and pressures up to 9 bar.

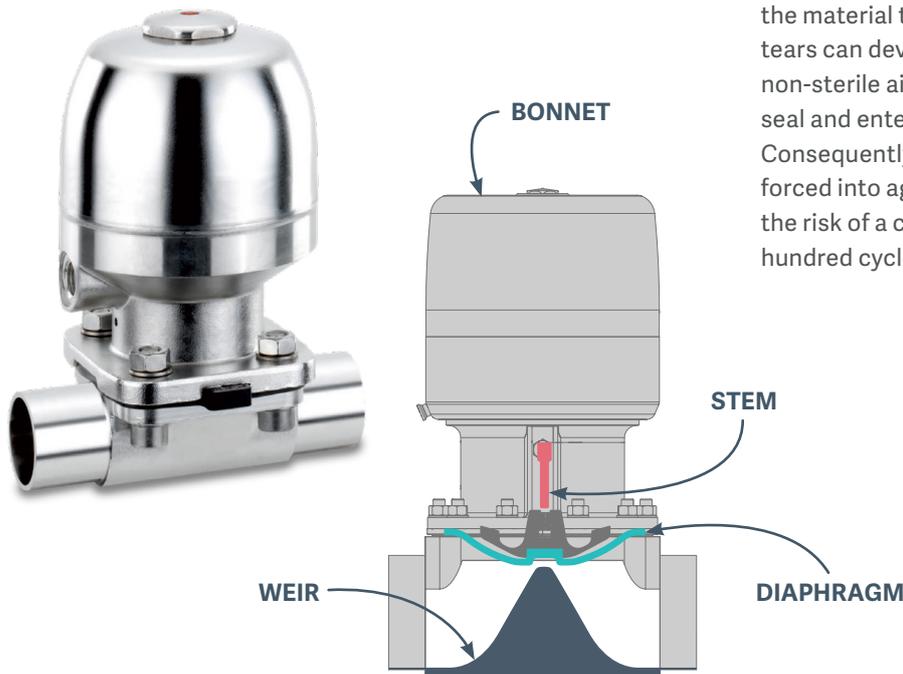
## Glossary:

- **ASME BPE:** American Society of Mechanical Engineers, Bioprocessing Equipment standards; the primary global standard for equipment used in sterile drug manufacturing.
- **Aseptic Processing:** Methods used to maintain the sterility of a product or environment throughout a process.
- **Bioburden:** The number of microorganisms living on a surface that has not yet been sterilized; a critical metric in validating sterilizer efficacy.
- **Bonnet:** The upper portion of a valve assembly that houses the stem, seals, and actuator components.
- **Cold Flow:** The permanent deformation of a material, specifically elastomers, under constant mechanical stress and high temperatures.
- **Dead Leg:** An area in piping where fluid can stagnate, potentially harboring bacteria or preventing full sterilization.
- **EPDM (Ethylene Propylene Diene Monomer):** A synthetic elastomer used for valve diaphragms that is valued for its flexibility but is susceptible to cold flow and thermal fatigue during repeated steam sterilization cycles.
- **Elastomer:** A polymer with elastic properties used for flexible seals; in sterilization, these materials are prone to thermal fatigue.
- **cGMP (Good Manufacturing Practice):** Regulatory standards (such as FDA 21 CFR Part 211) ensuring products are consistently produced and controlled to quality standards.
- **Log Reduction:** A mathematical term showing the relative number of live microbes eliminated; a 6-log reduction (99.9999%) is the standard for validated sterilization.
- **Piston Valve:** A linear-motion valve using a stainless-steel piston and self-adjusting gland packing to regulate flow.
- **PTFE (Polytetrafluoroethylene):** A high-performance fluoropolymer used as a chemically resistant face for diaphragms; while more resilient than pure elastomers, it is prone to reduced service life when exposed to high temperature fluctuations and flex-fatigue in high-cycle steam applications.
- **SIP (Sterilize-in-Place):** The use of clean steam to sterilize internal equipment surfaces without disassembly.
- **Stem:** The rod that transmits motion from the actuator to the valve's internal closing element (piston or diaphragm).
- **Weir:** The raised internal surface in a diaphragm valve body that the diaphragm presses against to shut off flow.
- **WFI (Water for Injection):** Ultra-pure water used in pharmaceutical production that must meet strict microbial limits.

## The Diaphragm Dilemma:

### Traditional Design vs. Modern Reality

When properly specified, installed, and maintained, diaphragm valves can perform effectively in many hygienic applications. In fact, diaphragm valves have been the default choice for many hygienic applications for decades. The appeal of the diaphragm valve has historically been its weir design, where a flexible elastomer membrane acts as a static seal. This design is intended to isolate the valve bonnet and internal mechanics from the sterile process media.



## The Weak Point: Bonnet Contamination Risk

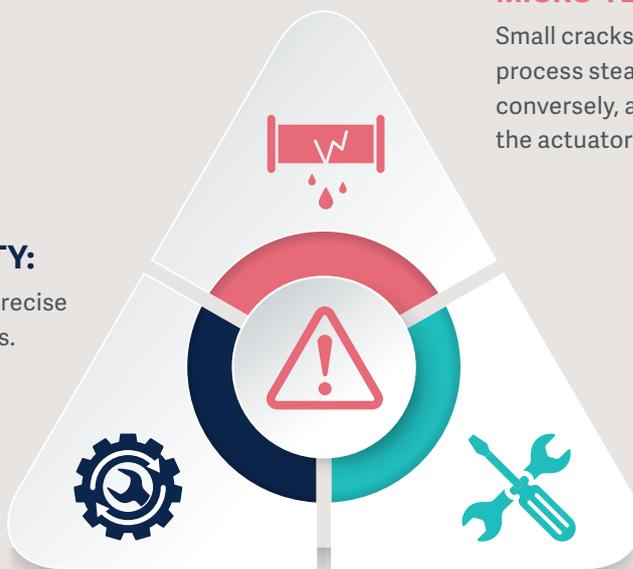
Diaphragm valves can be validated successfully. However, the risk increases under frequent thermal cycling and vacuum transitions. In a diaphragm valve, the bonnet, which contains lubricants and moving mechanical parts, is not part of the sterile flow path. It relies entirely on the integrity of the elastomer.

Under the intense thermal cycling of a cGMP sterilizer, the diaphragm undergoes cold flow and compression set. As the material thins and loses its elastic memory, micro-tears can develop. This creates a high-risk scenario where non-sterile air or bonnet lubricants can bypass the failed seal and enter the sterile chamber during vacuum phases. Consequently, facilities using diaphragm valves are often forced into aggressive maintenance schedules to mitigate the risk of a catastrophic batch failure, often within a few hundred cycles in high-frequency SIP applications.

## Diaphragm Fatigue Risks:

### TORQUE SENSITIVITY:

Diaphragm valves require precise torquing of the bonnet bolts. If done incorrectly, the seal may leak; if over-torqued, the diaphragm's life is shortened.



### MICRO-TEARS:

Small cracks can develop, potentially allowing process steam to enter the bonnet or, conversely, allowing non-sterile lubricants from the actuator to enter the sterile chamber.

### MAINTENANCE INTENSITY:

To prevent catastrophic failure, facilities are often forced into aggressive preventive maintenance schedules, replacing diaphragms at relatively frequent intervals in high-cycle SIP environments.

## The Piston Valve: Engineering for High-Cycle Sterility

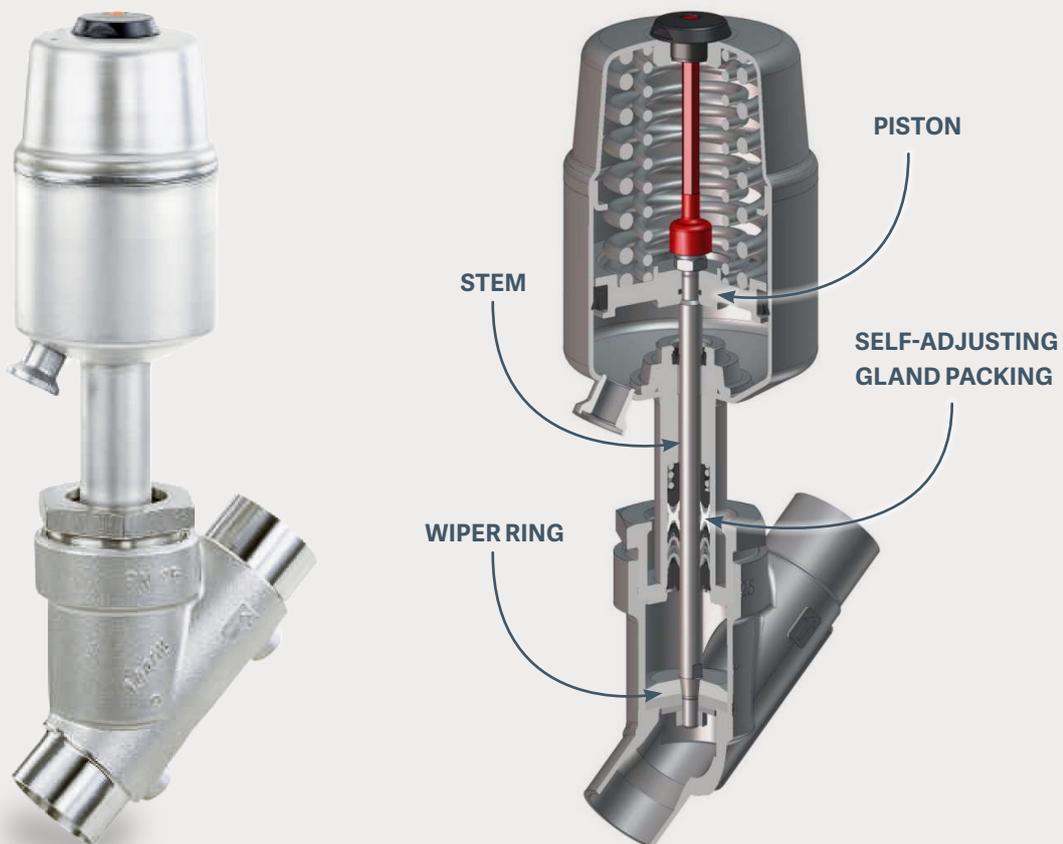
Modern piston valves, such as pneumatically operated angle seat globe valves, are engineered specifically for the rigors of high-pressure steam. Unlike the passive seal of a diaphragm, which merely sits against a weir, the piston valve utilizes an active sterile boundary.

### The Active Sterile Boundary

Piston valves utilize an active, self-adjusting, gland packing and a precision-engineered wiper ring. While critics of this technology often worry about the sliding stem of a piston potentially harboring contaminants, this concern is addressed by the sterilizer's own process logic. In validated Getinge cGMP sterilizer configurations, process logic can maintain continuous steam exposure (e.g., approximately 3 bar) at the stem during critical phases. This ensures the stem is continuously sterilized, creating a dynamic barrier that prevents microbial ingress and is often more robust under high-cycle conditions. However, this does not eliminate the need for proper service and maintenance, which are required to maintain aseptic performance, particularly around the stem seal.

## Proactive Bioburden Management

A primary concern in pharmaceutical manufacturing is the accumulation of bioburden within the crevices of process equipment. Critics of piston valves for cGMP applications often point to the stem-sealing area as a potential site for microbial buildup. However, the high-velocity clean steam utilized during the SIP phase ensures that the open state allows steam to circulate freely around the piston head and the lower portion of the stem. This rigid geometry ensures consistent thermal distribution and helps support validated SIP cycles designed to achieve a 6-log reduction of microbes.



# Operational Advantages

## Demonstrated Mechanical Durability

Because they utilize a robust stainless-steel actuator and piston rather than a flexible membrane, piston valves are built for high-cycle industrial service. They are effectively immune to the flex-fatigue that plagues diaphragm designs. This durability allows the valve to maintain a reliable seal even after a long service life in demanding steam applications, extending the time between maintenance intervals.

## Precision Control and Saturated Steam Quality

To ensure a validated outcome, a sterilizer must manage steam and condensate flow with extreme precision. Piston valves provide fast and accurate actuation, making them far better suited for modulating flow than weir-style diaphragm valves. This precision helps maintain the precise temperature-pressure relationship required for saturated steam, ensuring there are no cold spots in the chamber that could compromise the  $10^{-6}$  SAL.

## Vacuum Stability

A critical phase of cGMP sterilization is the pre-vacuum air removal. Piston valves are suitable for deep vacuum applications down to 20 mbar (a) when properly specified and installed. Their rigid construction ensures the seal remains stable under high negative pressure, whereas diaphragms can occasionally deform, leading to inconsistent vacuum levels and longer cycle times.

## Industry-Specific Benefits of Piston Valve Integration

While the mechanical advantages of piston valves are universal, their impact varies across different cGMP-regulated sectors. Understanding these nuances is essential for tailoring a sterilization strategy to specific production goals.

## Biotechnology and Large-Molecule Manufacturing

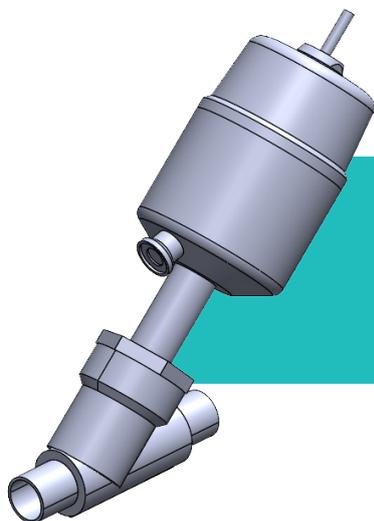
In the biotech sector, where batch values can reach millions of dollars, the risk of a failed cycle is a major operational threat. Diaphragm valves in high-cycle SIP systems are prone to losing their seal integrity during long steam exposure times. Piston valves provide the mechanical over-engineering necessary to ensure that 24-hour sterilization cycles are never interrupted. Their ability to handle high pressures without material fatigue makes them the ideal choice for protecting the high-value yields found in monoclonal antibody and vaccine production.

## Pharmaceutical Fill-Finish Operations

For manufacturers of injectable drugs, the primary concern is the prevention of particulate or chemical contamination. As diaphragms age and undergo thermal cycling, the elastomer can begin to shed microscopic particles, a phenomenon that poses a risk to product purity. The stainless-steel construction and hard-seal design of a piston valve provide a cleaner long-term solution, ensuring that the sterile boundary remains intact without introducing degradable materials into the flow path.

## Medical Device Manufacturing

Sterilizing complex pharmaceutical or biotech loads or porous loads requires deep vacuum pulses to remove air from internal lumens and crevices. The rigid construction of a piston valve ensures that these vacuum levels (down to 20 mbar) are reached quickly and held consistently. This stability directly reduces dwell time between pulses, effectively shortening the overall cycle time and increasing the daily throughput of the facility.



INTEGRATED  
CONTROL

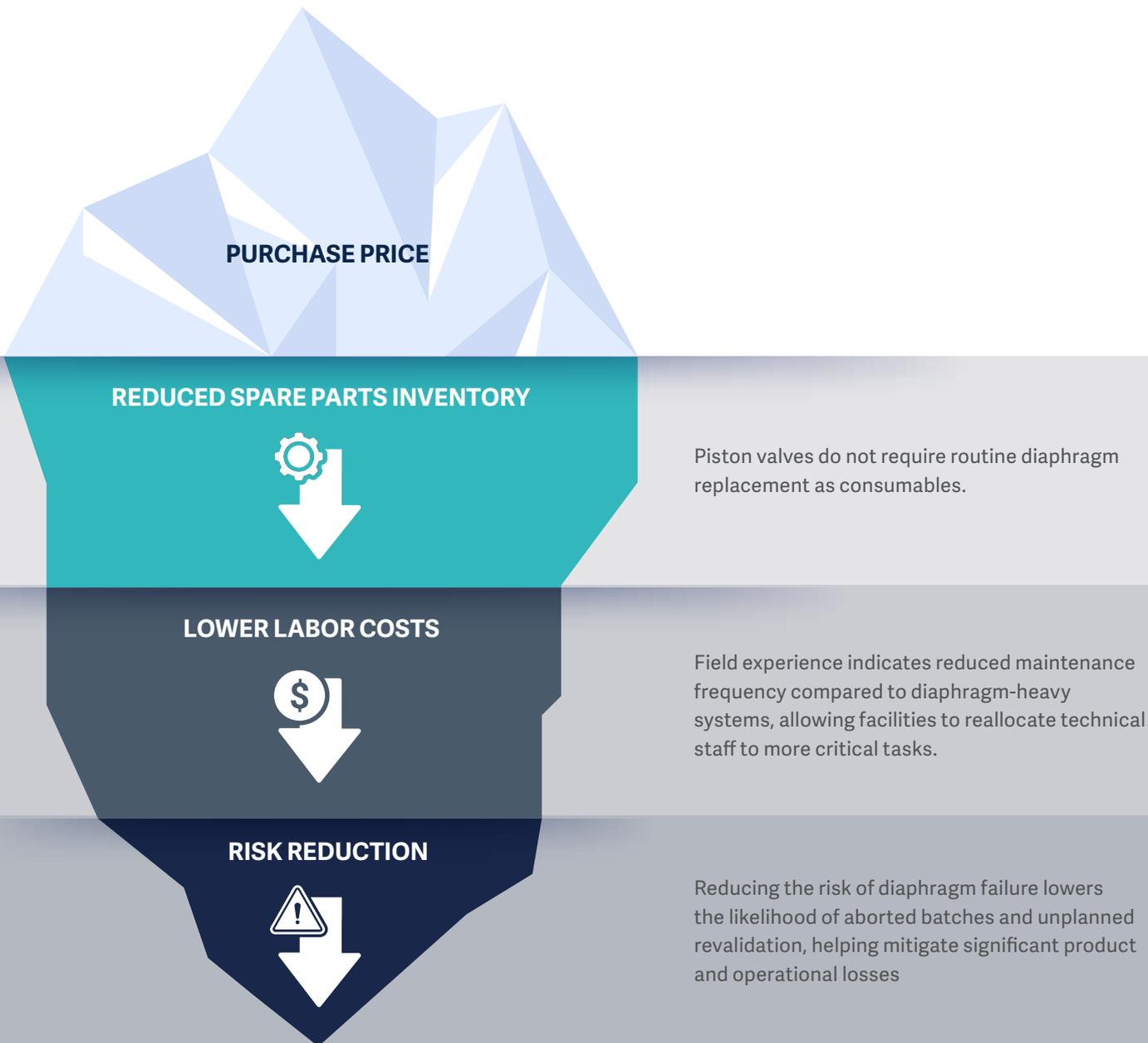


# Total Cost of Ownership (TCO) and Lifecycle Benefits

When evaluating valve technology, the purchase price is only a small fraction of the total cost. The TCO of a piston-valve system is often lower.

# Regulatory Compliance

Piston valves can be specified and integrated to meet the hygienic design expectations of the FDA, EU cGMP, ASME BPE, and EHEDG.<sup>2</sup> Their cleanability and material traceability (using 316L stainless steel and investment casting) support robust validation protocols.<sup>3</sup> While piston valves do not eliminate the need for revalidation, they do help reduce the need for revalidation due to component degradation.



# Conclusion

While diaphragm valves remain a viable option for simple, low-temperature applications, they often represent a higher-risk component in a high-performance cGMP sterilizer. The piston valve offers a superior alternative, providing the mechanical strength to handle high-cycle steam without the risk of elastomer fatigue. Ultimately, the aseptic integrity of a valve is not determined by its static design alone, but by its ability to be effectively and repeatedly sterilized in a high-cycle environment. By managing bioburden through active steam barriers rather than relying on a fragile elastomer, piston valves provide a higher degree of long-term aseptic security.

Diaphragm valves can still be incorporated into the process system if required by the customer, despite their known limitations. However, their use is not recommended for applications with continuous steam exposure, such as incoming steam valves.



## Surface Finishing Standards in Steam Sterilizers for cGMP Environments

Surface finish is critical to aseptic integrity. Learn how surface roughness (Ra) impacts cleanability and microbial adhesion in your GMP sterilizer.

Download the Application Brief: [getinge.com/dam/life-science/documents/english/sterilizer-surface-finishing-standards-applicationbrief-108476-en.pdf](https://getinge.com/dam/life-science/documents/english/sterilizer-surface-finishing-standards-applicationbrief-108476-en.pdf)



Surface Finishing Standards in Steam Sterilizers for cGMP Environments

APPLICATION BRIEF

GETINGE

## Getinge Biopharma cGMP Sterilizers



### GSSP Steam Sterilizer

A high-performance cGMP autoclave designed for component sterilization in biopharma production. It features sanitary stainless-steel construction (robotically welded chamber, satin-finished fascia) for easy cleaning, and offers chambers from 0.4–9 m<sup>3</sup> with multiple control options (Siemens, B&R, or Allen-Bradley). A SIMATIC WinCC Unified interface ensures intuitive operation across cycles. This sterilizer's validated design and global support network help manufacturers maintain uninterrupted, contaminant-free processes.



### GEV Steam/Air Mixture Sterilizer

Designed for cGMP compliant terminal sterilization of pharmaceutical products that must be dry and ready for further handling immediately after the cooling phase. It uses a combination of steam and compressed air to maintain chamber pressure, allowing heat-sensitive containers such as vials, glass bottles, and flexible bags to be sterilized without risk of deformation. The GEV provides rapid and versatile terminal sterilization pharmaceutical production environments where process reliability and throughput are critical.

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