

SELECTING MODULATING VALVES AND CLEAN STEAM TRAPS FOR STERILIZATION IN PLACE (SIP) SYSTEMS

by

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ABSTRACT

In today's pharmaceutical systems, SIP processes are becoming more and more critical. The nature of batch processing and the relationship between time and temperature for sterilization demand highly efficient SIP processes. The associated valves and steam traps must perform with high efficiency while meeting the stringent cleanliness requirements of the pharmaceutical and biotech industries.

This article will discuss key elements of control valve, pressure regulator and steam trap design for use in clean steam systems. Design considerations, selection criteria and performance expectations will be reviewed to further assist engineers and users during the specification process.

SIP SYSTEMS – A SHORT OVERVIEW

Pharmaceutical Sterilization-in-Place (SIP) systems are designed to sterilize a collection of process equipment after a batch of product is completed. Equipment such as bioreactors, fermentors and the accompanying tubing must be cleaned and/or sterilized before a new production cycle can ensue. These systems are constructed from high grade stainless steel materials as well as from FDA or USP approved flexible materials (i.e. Teflon® - lined piping).

The steam pressures seen are typically in the 20-30 psi range with corresponding temperatures ranging from 121°C to 135°C. The relationship between pressure and temperature is a given, however sterilization times will range depending on the temperature and the nature of the item being sterilized. In general, the lower the temperature, the longer it takes to sterilize. The sterilization time/temperature relationship in a typical SIP process will occur at about 121°C for 30-40 minutes. For systems with hard to reach componentry, times can increase.

Steam quality is also an important consideration. Typically, a dedicated clean-steam generator is used to provide the necessary volume, temperature and pressure of steam needed to sterilize each system. To ensure that each component and all areas of the piping reach the sterilization temperature for the requisite time, temperature sensors are placed in critical areas as well as in hard-to-reach locations to ensure that complete sterilization occurs. During this entire process, modulating valves are utilized to maintain the required clean steam pressure, temperature and flow levels.

During the SIP process, condensate is generated from steam which must be quickly removed. Proper placement of clean steam traps will ensure timely and adequate removal of the condensate, which, in turn, will help to maintain the high temperatures needed for the sterilization cycle.

A variety of other components are utilized, such as micro-filters, air vents and steam shut off valves.

Besides the critical function of the clean steam generator, three components in particular are crucial to maintaining adequate wet temperature in SIP networks: sanitary control valves, sanitary pressure regulators and sanitary steam traps.

SANITARY PRESSURE REGULATING VALVES (PRVs)

Self operated pressure regulators are found in most SIP systems. Their simplicity in function is appealing as no external control signal is required. PRVs incorporate a force-balance design wherein the inlet pressure of the medium passes through the valve orifice and acts on a diaphragm. When the pressure acting on the diaphragm exceeds the spring setpoint, the diaphragm assembly throttles the valve towards the closed position and reduces the outlet pressure.

Design Criteria for PRVs

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Several key design criteria should be considered when evaluating a clean steam regulator, all or some of which also apply to other sanitary equipment.

1. **Corrosion Resistant Body and Trim**

Typically, 316L grade stainless steel is used. This material is an excellent choice for the aggressive nature of clean steam. 316L stainless steel is also used for its enhanced welding properties.

2. **Food and/or Pharmaceutical Grade Soft Goods**

The sealing materials should be approved by the local food and drug agencies. Most manufacturers provide elastomers conforming to the US FDA (US Food and Drug Administration) code Title 21, Paragraph 177 which permits repeated use in contact with food. More and more, however, these materials must also comply with USP code Class VI, Section 88. USP, or United States Pharmacopeia, is concerned specifically with pharmaceutical and biotechnology products and equipment and the testing requirements for USP Class VI elastomers are often considered much more stringent than FDA approved materials.

3. **Self-Draining Design**

This includes the absence of threads as well as hold up volumes in the medium contact areas. When threads or hold-up volumes are present, they can prevent complete draining or make cleaning and sterilizing more difficult, presenting opportunities for bacterial growth inside of the valve which can contaminate the process fluid itself.

4. **Clean-in-Place/Sterilize-in-Place (CIP/SIP) Design**

Several design aspects must be included for SIP applicability including corrosion resistant materials, temperature compatibility of elastomers and self draining design. Of particular importance for pressure regulators (and back pressure regulators) is the ability to ensure the valve remains open during SIP cycles. When pressure regulators operate with low setpoints (i.e. below 20 psi), normal sterilizing pressures may cause the valve to close and prevent the cleaning/sterilizing medium from reaching downstream piping. Various methods for ensuring the valves stay open in these cases are available and include manual locking pins, automated mechanical locking pins and automated pneumatic chambers in the actuator.

5. **Sanitary Process Connections**

The intent here is to deviate from common industrial threaded or flanged connections. Various connection types include male threads, sanitary flanges, tube-weld (butt weld), and clamp fittings. Typically, clamp designs are preferred to enable ease of installation and quick removal in cases of cleaning, repair or replacement.

6. **Surface Finish**

Typically, users require a smooth mechanically polished surface in such devices. A common surface finish specification is 20 RA μ -inch. Depending on the individual user or process, mechanical surface finishes of 8 RA μ -inch followed by electropolishing or passivation may be required. Because of this, cast parts are typically viewed unfavorably with the preference being either barstock or forged materials.

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Example of a Clean Steam Regulator

Selection Criteria for PRVs

Once the basic design of the PRV has been reviewed, the selection will follow. When choosing the proper sanitary regulator for your clean steam systems, performance of the regulator is of paramount importance.

An inherent aspect to any spring loaded regulator is a deviation from setpoint as the valve capacity increases. This phenomenon is often called ‘droop’ or ‘offset’, which is expressed as a percentage of the setpoint. For example, if the spring is set at 100 psi, but the actual outlet pressure observed is only 90psi, the droop is 10%.

As the valve capacity is progressively increased, the outlet pressure typically falls. This fall, or droop, in outlet pressure is caused when the set spring relaxes as the valve opens more. The key consideration is how much flow will pass through the valve before this offset is too great?

A well designed, properly sized sanitary pressure regulator should experience about 10% to 20% droop.

Droop is primarily determined by three things: spring rate, effective diaphragm area and stroke length. Because it is difficult for the casual observer to determine these from visual observation or review of a datasheet, manufacturers have created tables to indicate the CV at various levels of droop. (Note: Dimensional drawings and spring setpoint ranges can give some indication of effective diaphragm area and spring rates, but use caution when considering such information). A sample droop table is shown in Figure 1.

Mark 96	Set Pressure PSIG	Droop					Cv for Relief Valve Sizing
		5%	10%	15%	20%	30%	
1" 4.5 Cv 15 to 50 psi range	15	0.68	1.15	1.64	2.16	3.27	10.7
	20	0.83	1.47	2.16	2.89	4.5	
	25	0.99	1.81	2.7	3.67	4.5	
	30	1.15	2.16	3.27	4.5		
	35	1.31	2.52	3.87	4.5		
	40	1.51	2.91	4.46	4.5		
	45	1.68	3.29	4.5			
50	1.85	3.67	4.5				

Figure 1. Sample Droop Table

For your given flow requirement, select the valve which offers the highest CV at the lowest droop percentage. The reason behind this is that SIP cycles demand highly accurate regulators. Regulators which

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display high levels of droop will result in lower downstream pressures and thus lower temperatures. This, in turn, results in longer sterilization times, potential for incomplete sterilization and/or fewer production batches per year.

SANITARY CONTROL VALVES

The use of sanitary control valves typically involves modulating the flow to control either the pressure of the steam or the temperature – depending on the type of controller being used.

Various configurations have been utilized ranging from on/off valves reconfigured for control (i.e. ball or weir types) to sleeved pinch valves to linear plug/seat control valves.

This section focuses on rising stem plug and seat valves.

Design Criteria for Sanitary Control Valves

Design criteria for a sanitary control valve are similar those of a sanitary pressure regulator. Since a regulator utilizes a diaphragm assembly and a control often has a reciprocating stem, the stem sealing of a control valve requires further evaluation.

In sanitary control valves, there are two primary methods to seal around the stem: o-ring and diaphragm.

An example of each is shown in Figures 2 and 3 below

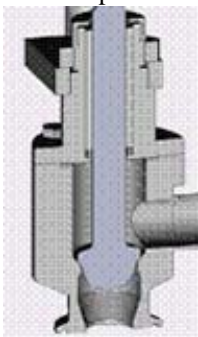


Figure 2. O-ring seal

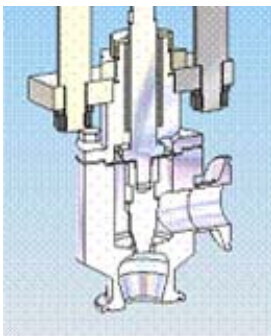


Figure 3. Diaphragm Seal

The primary benefit of the o-ring seal over a diaphragm seal is lower actuation force. Since the pressure of the medium in an o-ring sealed valve doesn't act on large diaphragm area, smaller actuators and lower air

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supply pressures can be used. Further, a variety of o-ring materials are readily available to allow users to customize the valve configuration to their process. For steam service, the use of perfluoroelastomers is rapidly increasing due to their high temperature resistance.

The drawback to the o-ring seal is that the stem reciprocates through the o-ring. During SIP cycles, the valve must be open which means portions of the stem will move above the sterilizing medium. For gas and steam services, this may be acceptable depending on the product being manufactured. Additionally, steam ports above the o-ring seal can be employed to ensure sterilization of the upper stem area. However, the trend among users is clearly moving towards the diaphragm seal.

With the two piece stem and plug assembly depicted in Figure 3, the diaphragm forms the external seal and, via compression, seals between the plug and stem. There is no reciprocation and all parts exposed to the medium when the valve is closed are also in contact with the medium when the valve is fully open.

Selection Criteria for Sanitary Control Valves

Once the proper valve design has been determined, several performance criteria should be considered prior to selection.

These criteria include:

1. **Continuous Steam Ratings**

For some diaphragm control valves, continuous steam service is limited to a range of 30-60 minutes at 20-30 psi steam. While this is sufficient to cover the demands of one SIP cycle, a better choice is to select a diaphragm design that has indefinite continuous steam service ratings. The diaphragm material in combination with the valve internal design will dictate diaphragm life.

2. **Closing Point**

A two piece stem and plug design shown in Figure 3 results in the plug closing against the valve orifice. Other diaphragm designs feature the diaphragm as the closing member. In such arrangements, the additional force required to seal, along with the increased velocities encountered at the vena contracta, often result in faster wear. In more rigorous steam applications, selecting the design which offers a dedicated seat seal and a separate dedicated diaphragm seal (for external sealing) will often enhance trim life.

3. **Flow Characteristic**

Following point #2 above, a dedicated plug seal and dedicated diaphragm seal helps to ensure a specific and consistent flow characteristic. The lower plug is contoured to yield a true equal percentage or linear flow characteristic. Designs utilizing a diaphragm as the stem seal and seat seal often display a non-linear or non-equal percentage characteristic or a characteristic which changes at various points in the stroke. A dedicated plug seal, also available with soft seals for Class VI shutoff, ensure excellent flow characteristics.

4. **CV vs. Travel**

In designs where the diaphragm seals against the seat, compression occurs. Moving from the closed position requires decompression of the diaphragm and this can consume portions of the input command signal, thereby reducing rangeability. On the higher end of the stroke, especially with weir style diaphragm designs, full controllable flow is typically realized well below the full open position. Maximum CV doesn't always relate to maximum controllable flow.

5. **Positioners**

The key aspect of a sanitary diaphragm control valve is the valve's internal, especially the diaphragm/plug assembly. Positioners produced by one valve manufacturer will typically work equally well on valves from an alternate manufacturer. In many cases, more cost effective options exist when the valve and positioner makes are not from the same firm. In modern Hart or fieldbus systems, a variety of positioner makes can be installed regardless of the control system brand without compromising communication or diagnostic functionality.

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When selecting your sanitary control valve, determine which factors are most important to you. In some cases you may find that a self-operated pressure regulator will meet your needs.

In regard to pressure control, three key benefits exist with control valves over regulators: higher flow capacities/turndown ratios, higher setpoints (primarily regarding pressure setpoints) and enhanced communication and diagnostics (via positioners).

There are places and needs for both types of products in a clean steam sterilization network, whether as part of an OEM supplied machine or as individual components in the SIP system.

SANITARY STEAM TRAPS

In older SIP systems, standard industrial stainless steel traps (or moderately modified SST traps) were often the primary choices for removal of condensate. The rationale was that the condensate was vented to a drain header and not further introduced to downstream process equipment. Currently, sanitary steam traps, also known as clean steam traps, have become more prevalent and are the subject of greater scrutiny.

Sanitary Trap Design Criteria

Much of the previously mentioned design criteria for valves apply to clean steam traps: materials of construction, surface finishes and drainability. The obvious difference is that clean steam traps do not have an external actuation device which causes them to open and close.

Various types of clean steam traps exist on the market today, including thermodynamic disc traps, float traps, fixed orifice traps and thermostatic element traps. Of these, the most commonly found type is the thermostatic element.

Two primary designs of thermostatic element traps exist with regard to the internal valve shape: ball and cone. An example of a ball type thermostatic steam trap is shown in Figure 4.

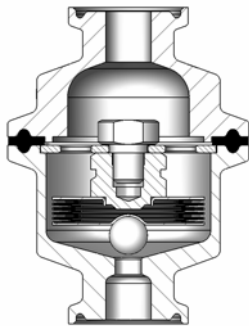


Figure 4. Ball Type Thermostatic Steam Trap

During sterilization cycles, trap capacity and subcooling are extremely important. Capacity simply means the amount of condensate, either in kg/h or lb/h, the steam trap can remove from the system. Subcooling refers to the temperature below saturated steam temperature at which the traps open. For example, if a thermostatic trap opens at 117°C and the saturated steam temperature is 121°C, subcooling is 4°C. Typically, users seek thermostatic traps which have the minimum amount of subcooling so that the lower temperature condensate is quickly removed, thereby contributing to efficient sterilization cycles.

There are two primary distinctions which differentiate the ball from the cone type configuration. These are:

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1. Flow Capacities

Very often, the ball type design will pass higher flow at similar subcool levels as smaller bellows movements result in a wider open orifice and higher flows. The cone-tip trap requires greater movement (i.e. more subcooling) to elicit the same open orifice area. While the size of the orifice certainly plays a role, the larger the orifice the greater the force the bellows must apply to shutoff. So, for the same sized orifice, a ball trap should pass more flow than a cone type. This also assumes the liquid fill in the bellows assembly is constant across designs. If the bellows assembly and orifice size are optimized, a ball type plug will yield higher flows at the same, or lower, subcooling levels.

2. Subcooling

Closely related to the capacity discussion above, a ball type design will often open at slightly higher temperatures than a cone type trap. The reason is linked to the orifice size. To reach equivalent flow capacities as the ball, the orifice of the trap typically must be larger. This larger orifice requires higher force from the bellows assembly. This higher force translates into greater subcooling before opening. Conversely, this greater force is achieved by selecting a bellows fill ratio that applies high force at lower temperatures. The result, is that the subcooling is typically greater for the given amount of flow generated by the opened orifice.

The two points above are closely linked. Bellows assemblies are proprietary to each trap manufacturer, so rather than attempt to ascertain which manufacturer offers better capacity/subcool characteristics, request detailed capacity and subcooling charts based on actual testing from the manufacturer to ensure the best trap performance.

TRENDS IN STERILIZATION SYSTEMS

As was mentioned at the beginning of the article, typical sterilizing temperatures are seen in the 121°C to 135°C range. However, some in the pharmaceutical industry have begun to embark on higher temperature sterilization cycles. High Temperature, Short Time (HTST) sterilization systems, with temperatures ranging from 140°C to 160°C, are becoming more commonplace in the biotech and pharmaceutical industries.

The impact this has on valve and traps can be seen in soft seal materials such as o-rings, diaphragm and gaskets. Especially noteworthy is the impact this has on diaphragm control valves. In already demanding applications, the design and material selection for these modulating valves requires close evaluation by potential users. Discuss this with your supplier when evaluating designs of various manufacturers.

A second trend which appears to be forthcoming is a more continuous process environment in pharmaceuticals. The FDA is beginning to address this movement through their Process Analytical Technology initiative. According to the FDA website, PAT is “a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.” This statement suggests a potential evolution towards more continuous processing (and potentially more continuous sterilization cycles) thereby requiring higher duty cycle diaphragm control valves for steam.

As the above develop further, larger valves for continuous service will be required, as will smaller valves for such equipment as mobile, modular clean steam generators and sterilizers.

SUMMARY

The bottom line is that valve and trap designs have evolved significantly since their inception two decades ago. Enhanced designs, new materials and demanding applications continue to emerge in the biotech and pharmaceutical arenas.

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As the populations continue to age and greater dependence is placed on pharmaceutical firms to generate new, cutting edge products, these drug companies will depend, in turn, on cutting edge valve solutions.

Consider a variety of aspects before selecting your next sanitary valve or trap and always keep an eye on the future.