TECHNICAL INFORMATION

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How to Specify Equipment for High-Purity Processes

Choosing the right combination of pumps, valves and seals is a crucial step in the design of fluid motion and control systems for the pharmaceutical and biotech industries.

Specifying the proper equipment and ensuring that this equipment works together in an efficient system can yield virtually contamination-free operation in high-purity processes. Coupling the right system of pumps, valves and seals with highly trained plant personnel will ensure successful operation for applications that demand the highest levels of purity and safety.

In the pharmaceutical, biotech and food processing industries, ingredients are transported, mixed, heated and cooled assuming the assurance of product purity required by law and taken for granted by consumers. Process systems for these industries require a level of purity not found in other applications, so implementing the right systems of pumps, valves and seals is vital.

The inherent problems linked to high-purity processes can all be traced back to one root cause: contamination. Any “dead cavities,” corners, seams or obstructions that exist in processing equipment could produce potential areas for bacterial growth. For example, a poor surface finish contains microscopic peaks and valleys that can lead to unnatural biofilm buildup — the formation of a thin layer of surface bacteria. Also, leakage causes improper mixtures of ingredients, which in turn allows unwanted chemicals to violate the system. Other potential problems include rusting, particle generation and oil and grease contamination.

High-purity equipment must stand up to harsh cleaning procedures — from steam to caustic sodas and light acids — without compromising either the integrity of the product or the equipment itself. Surface finish must be tightly controlled and dead cavities must be limited, so that the flow of the cleaning agent can reach all parts of the system. This process makes cleaning procedures more effective.

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Specify Pumps with Polymers for Clean Operation

The key to the design and selection of pumps for high-purity process applications is the ability to withstand high temperatures, high pressures and corrosive liquids while maintaining clean operation and minimizing contamination. Pumps are available in a variety of shapes, sizes and configurations, but certain factors must remain constant for any high-purity application.

All wetted surfaces that come in direct contact with the flow of a high-purity pump must be manufactured from materials that will not corrode, rust or generate particles during severe with superheated steam or other harsh chemicals. Pumps that are constructed (or lined) with PFA or PTFE polymers have a higher resistance to corrosion, lower reactivity and better surface finish properties than pumps designed using metal alloys or glass. Studies show that accumulated normal biofilm buildup is far easier to remove from these materials than from stainless steel or other alloys. Polymers do not rust, offer very low particle generation, and are inherently pure without the need for refining steps (i.e., electropolishing and passivation) other materials require. Since the introduction of the first fully lined PTFE chemical process pump in 1968, polymers continue to provide the safest, most cost-effective solutions for pump materials.

Metallurgy Makes All the Difference for Clean Valves

The first step in choosing a valve for a high-purity application is to select the right valve type. Diaphragm valves are by far the most common design of choice for high-purity industries; their geometry does not trap or contain media, preventing contamination and cross-contamination and facilitating system clean-up. However, in some applications, such as fermentation, sterile steam and freeze-drying systems, ball valves are preferred over diaphragm valves. That's because they eliminate catastrophic seat failure, possess better flow characteristics and provide higher pressure and temperature limits, which can lead to higher system output, improved efficiency and a much longer cycle life.

After specifying valve type, metallurgy and surface finish preparation are arguably the most important factors to ensure valve integrity. Clean valves should be forged 316L stainless steel with tightly controlled chemistry and surface finish. Cast materials are more apt to have exposed pits, inclusions and other imperfections as their surface finish deteriorates over time.

Valve end connections, called pipe ends or tube ends, should be specified with a sulfur content between 0.005 and 0.017 percent to meet ASME guidelines and allow for clean, contamination-free welds for tube bore systems, where all valves are welded in place. The concentration of ferrite should be less than 5 percent to prevent an iron film from forming (rouging) on stainless steel surfaces in high-purity water and steam systems. Some companies recommend less than one percent ferrite concentration, but this issue is still up for debate. Many studies are showing that rouging is more closely linked to metal preparation and content of gas atmosphere in the system than to ferrite concentration.

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Surface finishes need to be tightly controlled on all wetted surfaces of the valve through procedures such as electropolishing and passivation. Electropolishing is the method of passing DC current (approximately five amps) through the metal, causing the high points of the machined surfaces to be chemically removed. Passivation is the chemical process used to form iron oxides and chromium oxides on the surface of the metal to promote chemical resistance to the water or other products. For high-purity processes, valves that have surface finishes with an Ra of no more than 20 micro-inches minimize biofilm buildup, while electropolishing can reduce the Ra to fewer than 10 micro-inches. However, electropolishing is more expensive and is not always required for every application.

Inside diameters of the valve components should be chosen with tube bore dimensions that precisely match the connecting tubing to prevent stagnant areas of water, or "puddles," from forming in the valve. If these puddles occur, they can harbor microorganisms and provide a starting point for biofilm buildup. Seats should be specified as PTFE, reinforced PTFE or Flurofill to ensure bubble-tight shutoff through the valve without corrosion, even under conditions of high-vacuum and high-cycle operation.

When installing a valve, one must ensure that it will not introduce any new contaminates into the system due to manufacturing, transportation or final installation. To prevent this, valves should be assembled in positive-pressure clean rooms, tested with helium, double-bagged and sealed to ensure the highest level of cleanliness.

Set Up Cleaning Systems

No matter how well the equipment works, the inevitable buildup of bacteria and other contaminates in any system is unavoidable. High-purity systems use batch processing and specialized cleaning systems to combat this problem. During batch processing, a certain amount of product is created. Next, the entire system is cleaned with heated steam or light acids before production resumes. This process prevents any carry over of dirt and bacteria between batches of product. Common cleaning systems include Steam-In-Place (SIP) and Clean-In-Place (CIP), where heated steam and light acids or caustic sodas are used to flush any contaminates out the system.

CIP and SIP cleaning methods safeguard public safety by preventing cross-contamination and keeping purity to acceptable levels. They prevent batch losses and enable sterilization-in-place by removing dirt deposits that impede mass transfer of steam to all wetted process surfaces. These cleaning methods can also protect capital investment in equipment by preventing crevice corrosion that occurs when an impervious layer of dirt impedes maintenance of the passive metal oxide surface on stainless steel.

To ensure sterilization, a typical cleaning cycle should include the following steps:

- Pre-rinse with cool saline solutions to reduce the dirt load.
- Decontamination through steam or other caustic materials.
- Intermediate rinse.
- Acid-wash to solubilize precipitated materials.
- Final rinse to remove all traces of cleaning agents.

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Keep Your Equipment Up to Code

Equipment specified for clean operation must be chosen to conform to certain standards set forth by organizations such as the American Society of Mechanical Engineers (ASME), the American National Standards Institute (ANSI) and the International Organization for Standardization (ISO). In food and pharmaceutical applications, pumps, valves and seals should also comply with U.S. Federal Drug Administration (FDA) regulations.

More specifically, clean valves should be specified to conform to ASME BPE (Bio-Processing Equipment) standards for metallurgy and should meet the specifications of USP Class 6 set by US Pharmacopoeia for elastomers used in seat materials. US Pharmacopoeia forms the basis of enforcement actions by the FDA. For high-purity seals, P3-A, a pharmaceutical standard organized by 3A Sanitary Standards, Inc., has become widely accepted.

High-purity systems also need to be validated, which can put a large administrative burden on companies to cross-reference all paperwork with Certified Material Test Reports (CMTRs) on key components of each piece of equipment. Choose pump, valve and seal manufacturers that include simplified codes on each piece of equipment with four critical traceability requirements, easily read and cross-referenced by an inspector to save time and money on exhaustive paperwork.

The goal of these standards and validation requirements is to increase the efficiency of the development, manufacturing and supply of products and services while maintaining safety for consumers. Different standards exist for various applications, and it is always a good idea to consult an expert when choosing equipment to meet these regulations.

Complement Training with Experienced Personnel

Once a system of pumps, valves and seals is specified, one critical question remains: Who will install, operate and perform maintenance on this equipment? No processing system is complete without highly trained plant technicians who can ensure safe and efficient operation of all parts of the system. Often, the most effective way to achieve this level of efficiency is to implement training programs for current employees, as well as hiring a few key personnel. The knowledge and expertise brought in by the new hires will complement current employees' intimate knowledge of plant equipment.

When specifying equipment, consult engineers or other experts in fluid motion and control to ensure that the right equipment is being purchased for each respective application. High-purity processes are very specialized, and different applications include varying pressure and temperature requirements, materials, standards and levels of sterility. No single pump, valve or seal is suitable for every application.

Designing systems to process pharmaceutical and biotech products requires a high level of purity that

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will only increase with new technology and applications. As equipment and standards for high-purity applications continue to evolve, knowledge of available options becomes even more important. With the right system of pumps, valves and seals operated by well-trained technicians, any plant can meet and exceed these heightened standards and produce a consistent, pure and safe product.

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