INTRODUCTION TO SEALING MIXERS IN THE PHARMACEUTICAL AND BIOTECH INDUSTRIES

by

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ABSTRACT

While other segments of industry have slowed the biotech and pharmaceutical industries are emerging as strong growth industries. To participate in this promising growth the mechanical seal manufacturers have begun to focus their efforts on creating products that will more adequately meet the needs of these industries. While the basic mechanical seal has not significantly changed, there are design refinements that assist the biotech and pharmaceutical industries in producing the highest quality product possible.

When discussing mechanical seal designs for mixers it is important to understand that the pharmaceutical and biotech industries have some fundamental application differences. The general differences are summarized in Table 1.

Table 1. Comparison of Typical Operating Conditions Between Pharmaceutical and Biotech Mixers.

Operating Conditions	Pharmaceutical	Bio-Tech
Temperature	minus 200°F to 400°F	80°F to 105°F
Pressure	vacuum to 300 PSIG	zero to 15 PSIG
Shaft Speed	zero to 3600 rpm	zero to 150 rpm
Shaft Size	1" to 14"	1.5" to 6"
Entry Position	Top	Bottom
Sterile Operation	not necessarily	yes
Batch Operation	often	yes
Batch Type	various chemicals	cell cultures
Cleaning Conditions		
Cleaning media	mild chemicals	mild chemicals
Temperature	ambient to 120°F	ambient to 120°F
Sterilization	not necessarily applicable	required
Sterilization media	n/a	steam
Sterilization temperature	n/a	270° to 290°F
Heat Soak Time	n/a	20 minutes to 1 hour
Materials		
FDA compliant or GRAS	not necessarily	usually
USP Class VI compliant	not yet	coming on strong
Metallurgy	high alloys	300 series stainless steel

It may be surmised from the information in Table 1 that the pharmaceutical industry has as wide a variety of applications as the chemical industry. It is also clear that the biotech industry has comparatively mild operating conditions. Care should be taken to avoid quickly judging that biotech applications are easier to seal. In fact, there are conditions and requirements that make the biotech industry mixer sealing an interesting and challenging chore.

The top entry mixer still dominates the mixer marketplace. Top entry drives are used in gold and nickel processing, chemical and petrochemical plants, paper plants, and heavily used in pharmaceutical plants. This paper is limited to sealing slow speed top and bottom entry mixers, that is, mixers with shaft rotational speeds of 350 rpm or less, used in the pharmaceutical and biotech industries. In an attempt to avoid confusion, and while there are many similarities between the pharmaceutical and biotech industry, this paper will separate the discussions about these two industries.

PHARMACEUTICAL— TOP ENTRY MIXER APPLICATIONS

The top entry mixer applications used in the pharmaceutical industry tend to be similar to other process industries—the variety of chemicals, temperature, and pressures are diverse.

For instance, there are a variety of solvents used in pharmaceutical production that would not normally be thought of as acceptable materials for human consumption. Chemicals such as formaldehyde or acetone are unacceptable chemicals to ingest or inject into our bodies, yet these chemicals are used in the intermediate stage of production of pharmaceutical products. These chemicals are completely removed from the final pharmaceutical product.

Temperature extremes in the chemical and petrochemical plants tend to be toward the high temperature regime. Unlike the chemical processing industry the pharmaceutical industry has an ever-increasing requirement for operating in the cryogenic regime. This requirement is often to control vapor pressures or chemical reaction speeds of the product in the vessel. The parts of mechanical seals that are the most sensitive to temperature are the secondary seals, or the sliding gaskets, in the form of O-rings.

For high temperature applications there are many elastomeric materials from which to select a secondary seal.

There is an array of fluoroelastomers and perfluoroelastomers that have good high temperature characteristics that are perfectly adequate for pharmaceutical applications. However, care must be exercised in the selection of these materials when considering low temperature applications. The weakness of fluoroelastomeric and perfluoroelastomeric seals is that their low temperature capabilities are very limited. Perfluoroelastomers are not useful below zero degrees Fahrenheit. At subzero temperatures perfluoroelastomers become brittle.

Ethylene-propylene-diene-monomer (EPDM) elastomers are found in the pharmaceutical industry and are frequently used to extend the lower temperature limits of the mechanical seal and to tolerate steam cleaning. EPDM has a narrow band of chemical compatibility when compared to fluoroelastomers and perfluoroelastomers and should be selected with care.

Methods currently used for sealing cryogenic applications include:

- Utilizing flexible graphite secondary seals,
- Using polytetrafluoroethylene (PTFE) secondary seals,
- Using a close fitting metal wedge mechanically shrunk onto the mixer shaft, and
- Heating the areas of the seal where the secondary seals operate.

Keep in mind that balance of the components in the seal can easily tolerate cryogenic temperatures. We will return to this subject later—in a section about materials.

The pharmaceutical industry tends to use top entry mixers (Figure 1) for intermediate steps in the production of pharmaceutical products so it may not be necessary to sterilize the vessel and seal area of the mixer between batches. Cleaning the vessel and seal area in preparation for the next batch may be perfectly adequate.

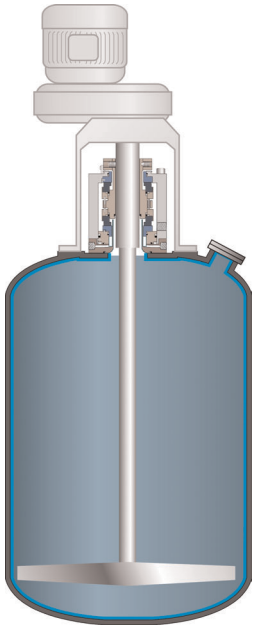

Figure 1. Top Entry Mixer Cross-Section.

Many companies have strict requirements for physical cleanliness of a batch so operational contamination must be avoided. This means that any normal day-to-day wear debris from the seal is not allowed to fall into the vessel. Another concern may be that the failure of the seal will cause excessive wear rates to the seal and introduce large amounts of seal debris to the batch.

The most common method of catching and capturing the debris before it falls into the batch is by the use of a debris "well" (Figure 2). The "well" is a passively designed "cup" that sits below wearing surfaces of the seal (Figure 3). It catches the debris from the wear faces before it falls to the batch.

The assumption is that the wear debris is heavy enough to fall to the bottom of the well due to gravity despite the small amounts of atmosphere motion in that area. Between batches when the product has been removed from the vessel, the debris is swept away using any number of flush procedures with gas or liquid.

The top entry pharmaceutical mixer has a long shaft with one or two impellers. The shaft must have a relatively large diameter to control deflection and vibration (Figure 4). Top entry mixers are easy to seal as long as the issues of runout, squareness, and vibration have been properly addressed in the design of the mixer. Pharmaceutical applications can be a variety of operating temperatures and pressures. It is important to note that as temperatures increase (or drop into the cryogenic range) and/or pressures start to exceed 200 psi, the need for a stable, low runout and very square

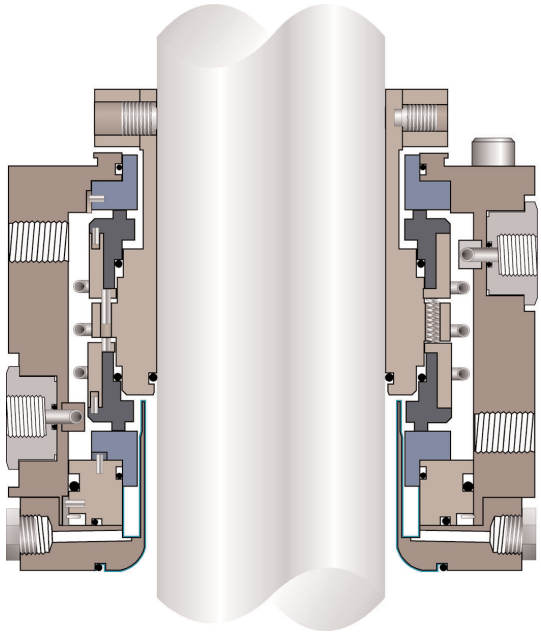

Figure 2. Cross Section of Dual Mechanical Seal with Debris Well for Top Entry Mixer.

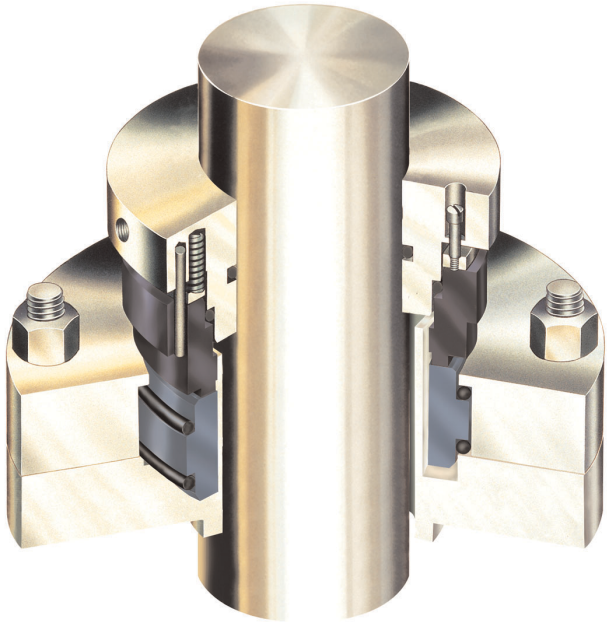

Figure 3. Single Outside Mechanical Seal with Debris Well.

mounting platform become more important to the proper operation and life of a mechanical seal.

Seal design is generally not the first consideration when a mixer is being quoted. To be competitive the diameter of the mixer shaft may be reduced along with other related dynamic components. As a result of reducing the shaft size the seal manufacturer is then asked to provide a bearing in the seal package. This increases the size and cost of the seal package. More importantly, it can dramatically affect the successful operation of the seal. The seal manufacturer must be vigilant in obtaining the direction and size of the forces on the bearing (and now the seal housing) so the housing, bolting, and bearing are not destroyed. A more subtle result of the bearing placement in the seal housing is the modification of the vibration characteristics of the mixer shaft and the location of the nodes in the shaft. Both can cause seal failure, and indeed the failure will be blamed on the seal design.

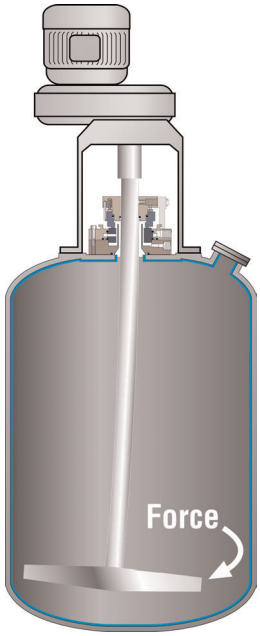

Figure 4. Mixer Shaft Deflection Due to Forces at Impeller.

The German Institute for Standards (DIN) calls for a bearing to be included in the seal package. The DIN standard also places a limit on the amount of forces that the seal package and bearing will be exposed to. In other words the stability of the seal platform is predetermined and small shaft sizes have *not* been selected to win the bid!

Bearings in the seal package have normally been designed to control radial forces. The radial forces must be carried down through the seal housing and the bolting, and ultimately to the vessel flange. Axial forces are difficult to control through the seal housing. If the pressures in the vessel are high enough to induce great thrust on the seal package then it is best to carry the force through the seal sleeve, directly into a thrust collar, and ultimately to the mixer drive thrust bearings.

The seal platform is the static and dynamic system on which a mechanical seal operates when attached to a mixer. The platform includes static installation concentricity and squareness, dynamic concentricity (runout) and squareness, waviness of the mixer flange, finish of the mixer flange, roundness of the shaft, finish of the shaft, vibration characteristics of the shaft and vessel, and thermal stability of the mounting flange and shaft. Typical finishes and dimensions of mixing equipment are as follows:

- Shaft roundness: ± 0.0005 inch
- Shaft diameter tolerance: ± 0.001 inch
- Shaft finish: 32 Ra or better

- Flange roundness: ±0.0005 inch
- Flange waviness: 0.001 inch TIR
- Flange diameter tolerance: ± 0.002 inch
- Flange finish: 64 Ra or better

- Assembly concentricity flange to shaft: 0.005 inch TIR or less
- Assembly squareness shaft centerline to flange seal mounting surface: 0.010 inch TIR or less

- Runout (operating concentricity flange to shaft): 0.015 inch TIR
- Operating squareness shaft centerline to flange seal mounting surface: 0.002 inch TIR

A very important fact often overlooked is the relationship between runout and squareness. As runout of the shaft increases the pendulum formed by the shaft with the pivot at the bearing increase the out-of-squareness of the shaft to the seal mount surface of the flange (Figure 5).

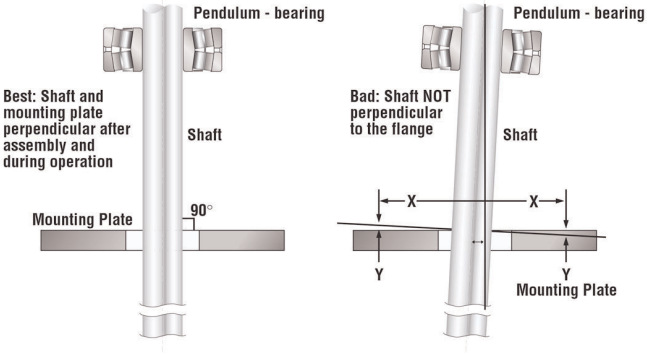

Figure 5. Shaft Deflection Translates to Squareness Problems.

Seal manufacturers have been designing for runout by increasing internal clearances for decades, but they have ignored the squareness relationship that is directly related to runout!

As pressures and temperatures increase, the user requirement to decrease leakage and increase life, shaft runout, and squareness have become vitally important!

If for instance a seal face lies 12 inches below a bearing, and using the bearing as the fulcrum we move the seal to an out-of-concentric position by 0.040 inch (0.080 inch TIR to the seal), this produces an angle of 0.2 degree. On a 6 inch shaft size this creates an axial TIR of 0.040 inch. This figure may seem insignificant until we realize that the secondary seals, whether O-rings, spring loaded plastic, or solid plastic, must slide against a metal component to accommodate this much movement. An oscillation of 0.040 inch TIR exceeds even the elastomer's ability to flex without sliding. Under even the best low temperature and pressure conditions this sliding will cause O-ring chafing and metal fretting. Under high pressure and/or temperature conditions we can expect O-ring nibbling, hang-up, and extrusion. All these effects will dramatically shorten the seal life.

A good target for equipment manufacturers that wish to maintain a high quality platform for the seal will design to a maximum 0.1 degree total out-of-squareness. There are seal designs that can tolerate up to 0.2 degree static or assembly out-of-squareness, but dynamically the issues of component wear and leakage still exist.

The most common single seal configuration for the top entry pharmaceutical mixer is the single outside dry running seal. Materials of construction are typically a resin impregnated carbon versus a ceramic face pair with 316 SS metal components and an EPDM or fluoroelastomer secondary seal. This seal operates as a contacting dry running seal and can typically operate at speeds up to 350 rpm and pressures up to 200 psi.

This seal may also utilize a debris well (Figure 6). The debris well piping connections are plugged or valved off during vessel operation. During cleaning the well can be swept clean by a flow of liquid or gas, commonly steam.

A properly operating seal on a 5 inch mixer shaft that operates to its full life expectancy may shed as much as 0.25 cubic inch of carbon over its life. That comes out to 0.0028 cubic inch of carbon per week, which is equivalent to a cube that is 0.141 inch to a side per week. These figures assume a 15,000 hour service life.

A common back-to-back configuration of a double seal for top entry mixers may be seen in Figure 7. This configuration is a flexible rotor design with built-in cooling.

Seal manufacturers can use this same general configuration to design a wet seal (barrier fluid water, ethylene glycol, oil, etc.), a dry running contacting seal (barrier fluid is a pressurized gas), or a dry running liftoff seal (faces are noncontacting during normal operation).

The double wet seal is a seal that has been widely accepted by the mixing industry. It is a seal that tolerates transient heat and pressure conditions well and maintains an absolutely positive seal

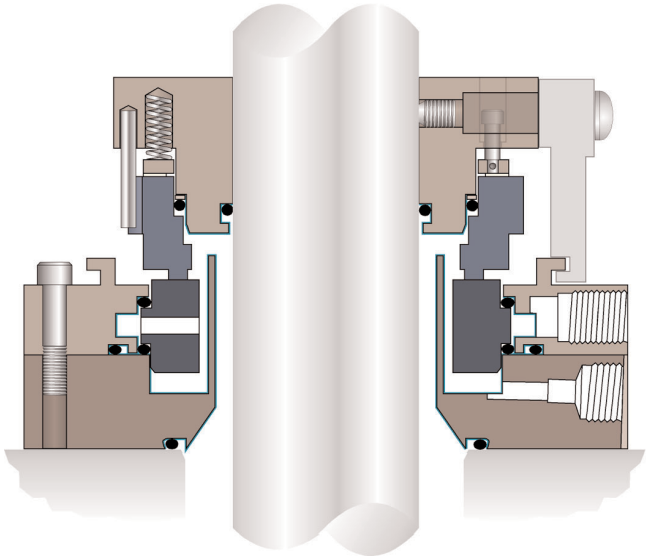

Figure 6. Single Outside Mechanical Seal with Debris Well.

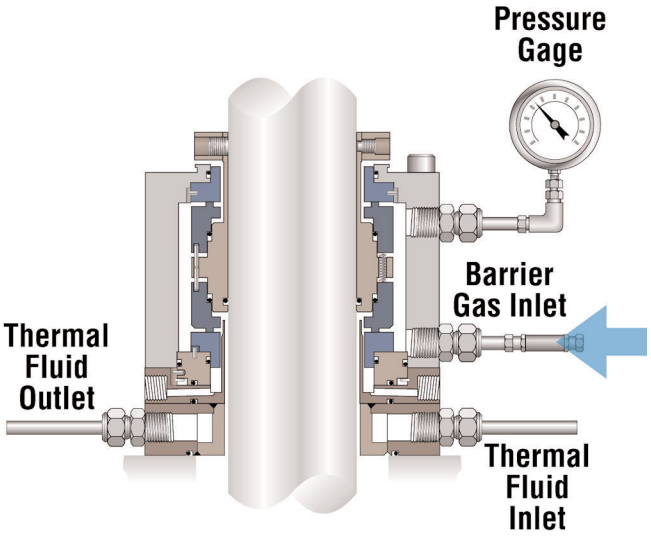

Figure 7. Cross-Section of Dual Top Entry Mechanical Seal with Cooling/Heating Spool.

between the vessel and the atmosphere. Nothing in the atmosphere gets into the vessel; nothing in the vessel gets out to atmosphere. It is easy to control the temperature of the seal cavity and surrounding area due to the application of a liquid barrier fluid. In a high temperature application a barrier fluid flow of liquid such as water can moderate the vessel heat soak to the seal and keep the seal's O-rings well lubricated and cool. In the case of cryogenics a liquid barrier fluid flow will keep the seal faces and O-rings warm and in a satisfactory operating temperature range.

Because of the desirable heat transfer and lubricating qualities of liquids, other methods can be applied to moderate the temperatures in the seal cavity when the vessel is either very hot or very cold. These include incorporating a cooling coil or a cooling jacket into the seal design. A cooling spool is also very effective at moderating heat flow. The "spool" design moderates the temperature in the seal cavity not so much by cooling or heating the seal cavity, but instead by blocking heat flow to or from the seal cavity. This approach is extremely effective in equipment with shafts below 6 inches diameter. As the equipment becomes larger, the shaft becomes a proportionally larger source of heat flow to the seal cavity. A cooling spool can only block heat flow through the housing area.

The cooling spool contributes a great deal to keeping the elastomers nearest the source of heat (or cold) at moderate temperatures. The moderate temperatures at the inboard O-rings contribute tremendously to the reliability of the seals. In certain operating conditions it has been found that use of the spool and cooling coil/heat jacket can allow the pressurized barrier fluid to operate with little or no flow. Since the spool and jacket remove heat from the sealing system the barrier system can be dramatically simplified. The high pressure barrier fluid can be introduced into the seal chamber with little or no flow.

The double dry seal is available in two designs: contacting and noncontacting. The contacting seal has, as the name implies, faces that contact and rub causing face wear. The hardware for the contacting seal has design features that are specific to the contacting seal faces because the load of the sliding surfaces must be precisely controlled. The cooling spool is of tremendous value in moderating the temperatures in the stuffing boxes but the cooling jacket/coils are of questionable use because of the gas phase heat transfer characteristics in the seal cavity. The contacting seal has temperature, pressure, and speed limitations that are generally reduced from the wet running seal.

The double dry noncontacting seal is designed similarly to the dry contacting seal, but the difference is that the faces are designed to have hydrostatic separation. The seal must have a predetermined pressure differential to provide lift because mixer shaft speeds are too slow to provide hydrodynamic lift. If the pressure differential is not maintained then the faces contact, the wavy face fills with debris, and wear accelerates to failure. The operating platform for these seals must be very stable for long seal life. A noncontacting mechanical seal tends to allow more gas through the faces. If the vessel fills with gas from across the inner seal it can be expected that the pressure differential will be lost and failure is imminent. This seal is capable of higher speeds and pressures than the contacting dry running seal and it can be expected that on a properly designed platform it will have no wear debris to fall into the process.

MATERIALS OF CONSTRUCTION

Metals such as 316 SS may often be used, but where added corrosion resistance is required it is common to upgrade to alloy C-276. This is a high nickel alloy that stands up well to acids and caustics. It is also thermally stable with good heat conducting characteristics. It stands up well to large temperature swings but care must be taken in the design phase to accurately account for thermal expansion and contraction. Sometimes 20 SS may be required and may be applied. All the materials above are easily acquired as generally regarded as safe for incidental contact (GRAS) materials and readily available from multiple vendors. These materials may be electropolished and passivated.

Face materials consist of carbon graphite, silicon carbide, ceramic, or tungsten carbide combinations. For dry running contacting seals, one face will always be carbon. For liquid lubricated seal the tribological pair can be any combination including hard-on-hard faces. Of these listed materials, carbon is the only material considered to be a "soft" face, all others are generally spoken of as being "hard" faces. These materials are readily available in GRAS form and specifications should state if certification is required.

Secondary seals and/or gaskets are also available in GRAS compounds. Pharmaceutical applications do not necessarily require GRAS materials so caution should be exercised to order the appropriate certification. GRAS compounds will normally not be provided unless specifically called for by the purchaser. Certification will not normally be provided unless requested by the purchaser. Elastomers and gaskets cannot be electropolished.

There are many compounds available for a broad spectrum of applications. Most chemicals and high temperatures found in the pharmaceutical mixer can be matched up to an acceptable elastomer. The glaring exception to this statement is for cryogenic

applications where temperatures dip below −40°F. EPDM elastomers are satisfactory for use in temperatures down to −40°F. EPDM is also tolerant of steam so it is a naturally good material where steam clean-in-place (CIP) is utilized. Care should be taken with EPDM because it is not one of the more robust rubbers for use in a wide variety of chemicals.

Fluoroelastomers and perfluoroelastomers are very robust when required to stand up against a wide variety of chemicals, but have poor low temperature characteristics. The O-rings become hard, inelastic, and shrink when cold making them unsuitable for low temperature operation below 0°F. In the past perfluoroelastomers withstood steam poorly, but new compounds promise to solve this problem.

Silicone and fluorosilicone O-rings stand up to cold service better than EPDM compounds and retain their elastomeric characteristics in temperatures down to −100°F. Unfortunately these O-rings have a much narrower band of chemical resistance than even the EPDM elastomers. They also have physical characteristics that contribute to making them a bad mechanical match for use in mechanical seals. They are soft and extremely poor in environments where there is constant motion however slight.

Early on an attempt was made to use compressed graphitized foils as secondary seal. While this material is very acceptable in cryogenic temperatures, it has bad qualities for use in pharmaceutical applications. It is a "dirty" product that sheds graphite. This is unacceptable in the pharmaceutical industry. It also has poor elastic memory and does not stand up well when exposed to the constant deflection required in a mechanical seal. It also has very little compressive memory.

Another approach to materials in cryogenic secondary seals is to use gaskets manufactured from PTFE. This material easily withstands low temperatures and is compatible with an extremely wide variety of chemicals. PTFE works well in static gasket applications but is a relatively rigid material that limits its use as a dynamic secondary seal. It is so hard that it "hangs up" the portions of the mechanical seal that must float on the secondary seals. PTFE materials also tend to have a high coefficient of thermal expansion so with large temperature changes this material may shrink away from sealing surfaces.

To eliminate all sliding secondary seals it has been suggested that bellow seals be used in conjunction with a mechanically loaded metal wedge design. This method falls short on two counts. First the bellows is a very "dirty" design with many convolutions capable of trapping debris. Secondly, in an attempt to replace elastomeric or PTFE secondary seals, a metal wedge is driven into a tapered collar so that the wedge is driven into the shaft and a seal is formed. This type of metal seal is likely to cause shaft damage—if not during installation, then during removal. Mixer shafts tend to be very expensive.

The most successful method of sealing cryogenic services is still selecting the appropriate materials based on chemical compatibility and other service conditions and moderating the temperature at the secondary seals by use of barrier fluid, cooling spool, or cooling jacket/coils. These methods are particularly useful for research vessels and plants where various products can be produced in any vessel. Not only do these techniques work at keeping the secondary seals warm enough to operate properly, these devices can be used to lower the temperature on the O-rings when the vessel is operating at a very high temperature.

TOP ENTRY FLUSH PLANS

Single Outside Mechanical Seal—Plan 02 with Option for CIP or SIP

The single outside mechanical seal utilizes a single face set and is the simplest mechanical seal used on top entry mixers. During normal operation vapors from the top of the vessel will escape in some small amount, usually measured in standard cubic feet per hour, to the atmosphere. During the manufacturing operation the taps "A" and "B" are plugged and residue from the seal face settles into the bottom of the debris well (Figure 8). Once operation is complete the vessel is cleaned, and the well may also be cleaned. Steam of chemicals may be injected in port "A" and drained out through port "B" carrying any debris with it. Care must be taken to not inject a chemical that will deposit solids on or around the seal faces or dynamic elastomers. Care should be taken to not inject chemicals that will damage the materials of construction of the seal.

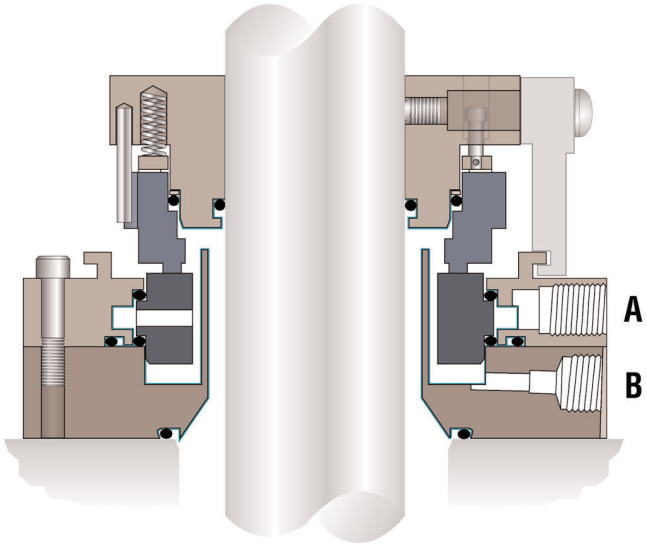

Figure 8. Top Entry Mixer Single Seal with CIP and SIP Features.

Plan 54 systems are used when dual pressurized liquid seals are required. This design is generally selected where leakage of process fluids to the atmosphere is not acceptable. Connections "A" and "B" are used to introduce barrier fluid into and through the seal cavity (Figure 9). Connections "C" and "D" are used to introduce a low pressure cooling fluid through the coils in the seal cavity. A cooling spool may also be used to control heat flow to and from the seal cavity (not shown).

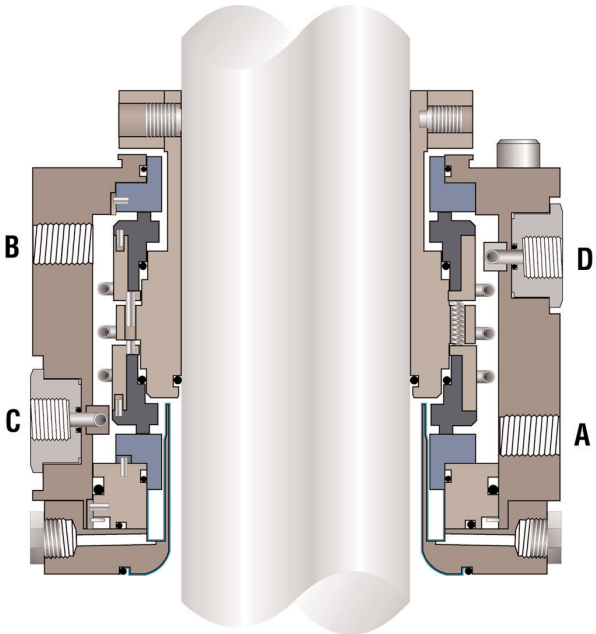

Figure 9. Dual Wet Mechanical Seal—Plan 54 with Options for CIP and SIP.

The success of a dual liquid lubricated seal depends on the creation of a good sealing environment in the seal cavity. The flow rate of barrier fluid will be dependent on the application, including speed, pressure, and vessel temperature, and whether the cooling coil is used. It is recommended that the pressure of the barrier fluid be 15 to 25 psi above the vessel pressure. The pressure of the water through the cooling coils need only be high enough to obtain the necessary cooling flow. The barrier fluid should be a cool, clean fluid, such as cooled steam condensate. The barrier fluid should also be compatible with the process since small amounts of barrier fluid will weep into the process through the inboard mechanical seal. The water in the cooling coils will not be in contact with the barrier fluid and will not escape into the product.

Plan 74 piping plans are selected when a dual pressurized seal is required but the process cannot tolerate liquid barrier fluid leakage into the vessel. Contacting dry seal designs may be selected to minimize the gas barrier leakage into the vessel keeping in mind that contacting gas seals are limited to lower pressure and speed. During normal operation port "A" is used to pressurize the seal cavity with gas, usually an inert gas such as nitrogen (Figure 10). Other gases may be used including compressed air. Port "B" is normally plugged. Steam may be used as a barrier fluid but port "B" must be opened and piped to create a steam flow-through condition. Often the steam is dead-ended into the seal cavity where the steam condenses on the cool shaft, housings, and seal components. The lower seal is then immersed in condensate and tends to leak inboard.

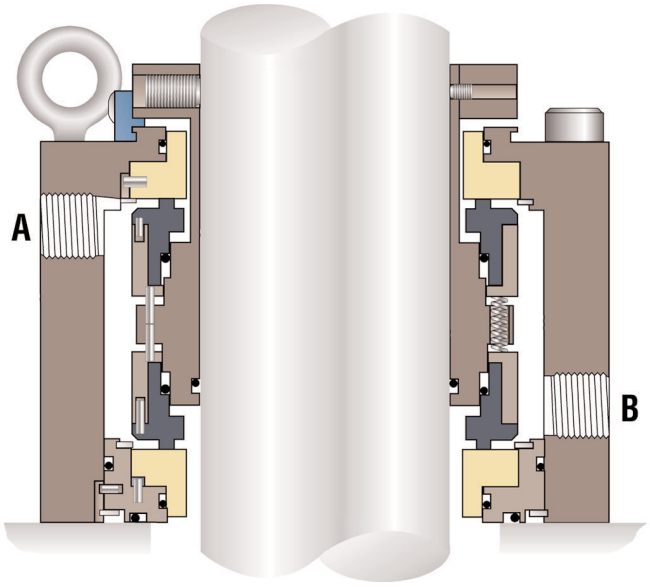

Figure 10. Dual Dry Contacting Mechanical Seal—Plan 74 with Options for CIP and SIP.

Plan 74 piping plans are also selected when a dual noncontacting pressurized seal is required but cannot tolerate liquid barrier fluid leakage into the vessel. The noncontacting face design can handle more speed and pressure but expected barrier gas leakage into the vessel and into the atmosphere will be greater than the contacting design. During normal operation port "A" is used to pressurize the seal cavity with gas, usually an inert gas such as nitrogen. Other gases may be used including compressed air. Port "B" is normally plugged (Figure 11). A minimum barrier gas differential pressure is required to assure face separation in a noncontacting design. Barrier gas pressure often must be at least 50 psi greater than the vessel pressure. Superheated steam may be used as a barrier fluid but port "B" must be opened and piped up to create a steam flow-through condition. Often the steam is dead-ended into the seal cavity where the steam condenses on the cool shaft, housings, and seal components. Condensate runs to the lower seal where it is pumped into the vessel.

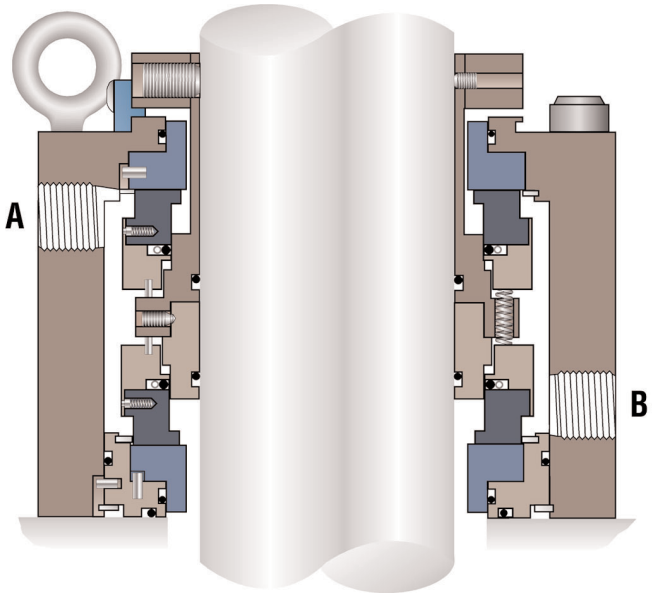

Figure 11. Dual Dry Noncontacting Mechanical Seal—Plan 74 with Options for CIP and SIP.

BIOTECH AND BOTTOM ENTRY MIXERS

The biotech industry is unique in that it processes living microorganisms in a factory setting. These organisms are not necessarily the product themselves, but the output of the organisms is used as an intermediate in the production of pharmaceutical products. Keeping these tiny organisms healthy while mass producing them is a demanding and expensive chore. Producing an environment to maximize health and growth is of key importance.

The biotech industry is leaning toward the use of bottom entry mixers. Bottom entry mixers have shorter shafts and require less headroom for maintenance. Like a pharmaceutical mixer or a chemical mixer it is desirable for the biotech mixer to evenly distribute various process components into a homogeneous blend. In the case of a chemical or pharmaceutical mixer the chemicals have abundant time to blend and react.

The biotech mixer must produce even distribution of various process components, however there are additional concerns. Keeping in mind that the product in a biotech application is alive, then it is easily understood that gases and nutrients must be introduced and dispersed to all the organisms at an optimized rate. It must also be considered that an organism can be damaged or destroyed if the shear rates are too high due to high impeller tip speeds.

Most pertinent to the selection and application of a mechanical seal is the fact that a clean-in-place or a steam-in-place (SIP) procedure is required for mixers in the biotech industry. The methods used to clean, sanitize, or sterilize the vessel and the mechanical seal can severely impact the ability of the seal to operate successfully beyond one batch. Historically CIP and SIP data were not adequately communicated or considered in the selection of a mechanical seal and sealing system.

It was discovered, often after a seal failure, that price and delivery played a larger role in seal selection than did the consideration of the cleaning conditions. In fact, cleaning conditions were often never considered in seal selection because there was little or no understanding of the biotech mixer operation that would incite the seal manufacturer to pursue these data.

MECHANICAL DESIGN

The bottom entry mixer drive typically has a shorter and more robust shaft and seal platform. Historically the available room for seal installation, including exposing a shaft-end to slip the seal over, has been limited. This has severely limited the seal design

and features that a seal manufacturer could recommend. Now the seal designer must attempt to design the mechanical seal to meet the needs of the biotech industry. As the designer learns more about the biotech industry, more features, and thus more room, are required for the sealing package.

Generally speaking, in the past the seal manufacturer gave little consideration to the cleanability of the seal. As a customary business practice purchasing agents may gravitate to the lowest price seal bid with no regard to future costs. This means that seal companies were strongly encouraged to offer cheap seals. This seemed like an acceptable practice simply because the operating conditions were very mild and the seal was removed during vessel cleaning and then the seal was replaced. However, the need for a more permanent seal installation that could stand up to CIP and SIP is recognized. Maintenance time and cost can be dramatically reduced if it is not necessary to disassemble the mixer after every batch. So in bottom entry mixers where the mechanical seal is immersed in the product, the mechanical seal must withstand various modes of CIP and SIP, and meet strict material-of-construction requirements.

In the past single seals have been used with rubber elastomers and/or single coil springs immersed in the product. By today's standards these are dirty designs and tend to harbor and incubate undesirable cell growth. These seals have an advantage of being inexpensive to the point of earning the reputation as throwaway seals. However, these seals require that the shaft end of the mixer be exposed for removal of the old seal and installation of the new seal. This can be a time consuming, and therefore costly, procedure.

The primary goals of a bottom entry biotech seal are:

- Complete drainability.
- No cracks or crevices for organisms to collect and incubate.
- Polished surfaces.
- Materials compatible with steam and cleaning chemicals.
- Accessible to vessel-side cleaning balls and washers.

Complete drainability must occur both in the vessel side of the seal and in the barrier fluid area inside the dual seal (Figure 12). While great strides have been made in accomplishing this goal, unfortunately it is currently impossible to have complete drainability. The necessity to seal the gaps between the seal sleeve and shaft and the seal housing and mounting flange cause there to be small undrainable areas in the seal/mixer interface. Also the internal areas of the seal present certain impossibilities for draining. It is impossible to properly slope all surfaces inside the seal canister.

A mechanical seal has many cracks and crevices that could act as incubators for cell growth. As with drainability there is concern that all these areas cannot be completely sanitized or sterilized. The internal portion of a mechanical seal canister has pressed-in pins, set screws, spring holes, and O-ring annulus. An additional crevice, one that is impossible to remove, is the gap between the rubbing faces where the lubricating fluid film resides.

Electropolishing can make it more difficult for debris and living organisms to grip surfaces. It is common for product side surfaces to be electropolished. Often the surface finish target is 15 Ra. It is important to note that electropolishing is generally regarded as capable of improving the surface finish by half. In reality when electropolishing finishes are mechanically polished to 32 Ra or better there will be far less improvement to the finish. To obtain better surface finishes when 32 Ra is called for mechanical polishing must be applied previous to the electropolish. The "half" rule applies to surfaces that are mechanically finished to no better than 64 Ra.

The surface finish of mechanically polished metal is different from the surface finish of electropolished metal. Microscopically the finish of a mechanically polished surface reveals tears, pulling, and shredding of the surface. A properly prepared and electropolished surface is microscopically featureless with no grain boundaries, free iron, or mechanical imperfections that are visible.

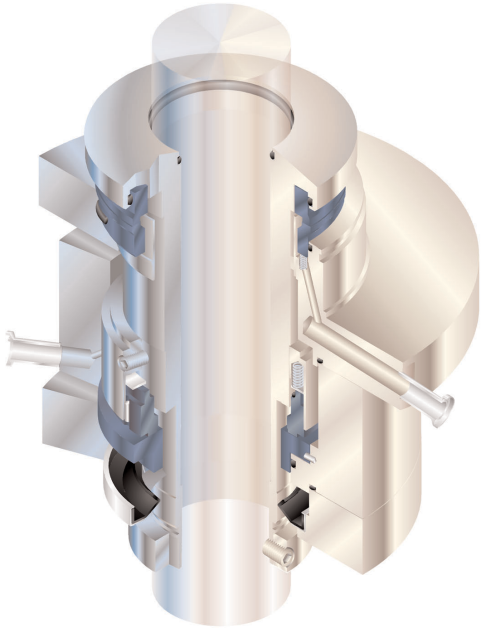

Figure 12. Dual Seal for Bottom Entry Mixer.

While most of the components that contact product of a mechanical seal may be electropolished it must be pointed out that there are materials that cannot be electropolished such as O-rings and gaskets. In the case of O-ring secondary seals and gaskets, the best that can be accomplished is to ensure that the cavities in which the O-ring sits can be opened up to expose as much of the cavity as possible for cleaning and/or sterilization. This technique calls for a large gap between the metal parts of the O-ring cavity and care must be taken that pressure will not extrude the O-ring through the gap.

The interior of the seal is subject to the same limitations as the product side of the seal, that is, there are many cracks and crevices for living organisms to hide from the cleaning/sterilization effort. Also there are additional materials used in the seal that cannot be polished to a desired 15 Ra finish such as O-rings, carbon graphite components, and ceramic components. There are machined areas of the seal that cannot be practically polished to the desired finish such as housing drill-through, milled slots, and threads in collars.

The best that can be accomplished for cleaning in the seal canister cartridge is to make as many drainable areas as possible and polish as many areas as possible to assist in the CIP and SIP process.

The materials of a mechanical seal properly selected for cleaning and sanitizing can have high expectation for success. Naturally, this requires that the person selecting the seal knows and understands all phases of cleaning and operation previous to making the seal selection. If the seal's materials of construction cannot tolerate the mild caustics or acids used to clean the vessel or seal cavity then damage may occur. With complete information it is a relatively simple task to select the proper materials or help guide the person who is specifying the equipment to a satisfactory selection.

Biotech application temperatures tend to be mild. However, the temperature of steam sterilization by steam injection into the vessel and steam injection into the seal can cause seal failures. In the past the seal manufacturer was not informed that steam was injected into the vessel and seal between every batch. If the person specifying the seal knows about the SIP then it is common to provide EPDM O-rings to withstand the steam, but it is possible

that there were no additional discussions regarding cleaning chemicals. Some of the cleaning chemicals are not appropriate for contact with the EPDM O-rings. It can be seen that the lack of information regarding *all* process and cleaning cycles could easily result in a seal misapplication.

BIOTECH MATERIALS OF CONSTRUCTION

Materials of construction must contain as many of the following attributes as possible:

- Compatible with mild caustics
- Compatible with mild acids
- Compatible with steam
- Shed no undesirable residue into process
- Free of porosity that may harbor cell growth
- Possess material qualities such as hardness, elasticity, tribological wear characteristics, etc., for general good and acceptable seal design and operation.

In the cleaning process, including CIP and SIP, there are three main solutions. The three solutions include caustic, acid, and steam. The most common caustic is sodium hydroxide, but also used are sodium metasilicate and phosphate compounds. The most common acid used for CIP is a mild concentration of phosphoric acid but nitric and citric acids are also used. Acids and caustics are used for CIP while steam is used for SIP. Caution must be exercised because caustics can leave a residue on the seal face or around the secondary seal areas. This residue can cause accelerated wear or hang up components that must remain mobile. Thorough flushing with deionized (DI) water is strongly suggested.

Steam is used for SIP and will typically be saturated steam at 131°C (267.8°F). However, steam and hot water may also be used for CIP at temperatures around 80°C (176°F)—a much more tolerable temperature for elastomeric O-rings. Steam is used in these applications where the steam is used to arrive at a target temperature on all surfaces to be cleaned or sterilized. Once the target temperature has been hit, the cleaning continues for a predetermined amount of time to make sure that all surfaces arrive at the necessary temperature.

Common metals such as 304 SS, 316 SS, and 316L SS all do well in the mild concentration and temperatures of acids and caustics mentioned above. Care should be exercised if it is desired to use nickel bound tungsten carbide with these chemicals. While tungsten carbides stand up well to caustics they may not fare as well when exposed to mild acids.

The most common face material, resin filled carbon, is readily available in grades that have good sealing qualities and stand up to all the chemicals and temperatures mentioned above.

Ceramics including silicon carbides tend to hold up well against these mild chemicals and steam. The main concern with ceramic is the possibility for thermal shock. Care should be taken to ramp the temperature of incoming liquid or gas to achieve a temperature rate of change gradient of 70°F/min or less. Taking note that as a hot (or cold) liquid moves from its source to the ceramic that the metal in tubing, piping, and adaptive hardware all contribute to absorbing heat out of the stream and therefore soften the thermal blow to the ceramic.

Fluoroelastomers stand up well to most chemicals except sodium hydroxide with some question about steam. Perfluoroelastomers stand up to the chemicals used for CIP, but do not do well in steam. Perfluoroelastomers tend to take a compression set in steam. There are new compounds being developed that are claimed to stand up very well to steam, almost as well as peroxide cured EPDM.

EPDM is a preferred choice by many due to its availability, cost, and ability to stand up to caustics and steam. EPDM falls short when asked to stand up to acids and hydrocarbons.

All the materials mentioned above are readily available as Federal Drug Administration (FDA) compliant GRAS materials. To be compliant with the GRAS callout simply means that the material does not shed any undesirable material into the product. In most cases the material has not been tested but instead the manufacturer of the material provides a list of the makeup components in the material and if no objectionable materials are used, or no history of usage problems exist, then the material is awarded GRAS status. This is not an FDA standard, but simply a guideline.

Another material requirement that is coming on strong is the United States Pharmacopoeia (USP) Class VI requirement. This requirement goes a step further than the FDA GRAS statement in that actual testing must be performed to determine the safety of the material. The material is injected into a live test animal and the animal is inspected after a specified amount of time for a reaction to the material.

It must be remembered that the FDA or USP is making no comment on the appropriateness of the material in the product or how it will react with the product, only that the material as a standalone product is safe within the stated guidelines of both requirements.

BOTTOM ENTRY FLUSH PLANS

Plan 54 systems are used when dual pressurized liquid seals are required. This design is generally selected in processes where leakage of process fluids to atmosphere must be eliminated. This seal is a bottom entry seal and is immersed in the process fluid in the vessel. Port “A” and port “B” may both be used for CIP and SIP (Figure 13). The shaft may be turning during CIP, usually at a reduced rpm, but during SIP it is recommended that the shaft be stationary.

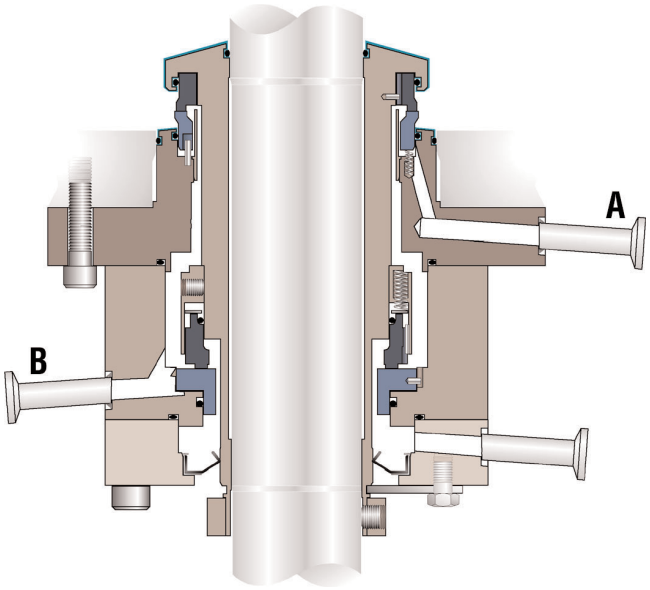

Figure 13. Dual Pressurized Mechanical Seal—Plan 54 with Option for CIP and SIP.

CIP

CIP is performed either as the single method of cleaning or as a predecessor to SIP for sterilization. It is important to note that CIP is generally regarded as a method that can be used to reach a state of asepsis, but not sterile.

Whether the vessel is a top or bottom entry vessel spray balls or spray arms will be used to introduce CIP chemicals into the vessel. They are designed to direct a blast of chemical at the vessel walls and around vessel wall intrusions such as hatches, strakes, or piping connections. The blast assists in breaking away residue and assuring that any corner or crevice is thoroughly cleaned.

A reflux method of CIP can also be used. In this case the CIP chemicals are evaporated in the vessel by the application of heat. The chemical "steam" then condenses on the cooler vessel wall and runs back down into the pool to be boiled into steam again. The selection of reflux or chemical spray is selected based on characteristics of cleaning that are determined most important. The reflux method does a better job of obtaining a state of asepsis in the vessel while the spray ball does better at removing masses of debris.

During CIP it is normal to rotate the mixer shaft slowly to expose all surfaces and corners to the cleaning solution. This means that the seal must be operated as if the seal were in service. Sodium hydroxide is the main alkaline cleaning compound used in CIP with varying degrees of sodium hydroxide concentration as well as sodium metasilicate and phosphates.

The seal flush should be continued during CIP. This assures that the seal is properly cooled and lubricated during the CIP process and that the seals will not be damaged. The flush will also help the faces remain free of precipitating caustic solution that might damage the seal faces.

Since sodium hydroxide can precipitate solids on seal faces it is desirable to keep the seal face flushed with clean barrier fluid. This ensures that residual sodium hydroxide will not harden between the sliding surfaces of the seal, or set up around the sliding secondary seals and cause seal hang-up. It is strongly recommended that during mixer drive and seal selection the seal vendor recommends an operating barrier or buffer fluid flow rate and temperature to assure that the seal is not damaged during CIP.

Often after the alkaline wash the CIP is finalized by a mild acid wash to neutralize the caustic. Note that the chore of the acid is to neutralize the chemicals in the vessel. This means that the acid is relatively mild and the exposure time of the acid to the seal materials of construction is short.

It is not normal to wash the seal cavity of a double seal with an alkaline solution. The seal cavity is normally free of debris. The risk of depositing solids on the seal faces by precipitated caustic outweighs the potential good that can come from flushing an alkaline solution through the seal. However, if the seal barrier cavity is flushed with an alkaline solution it is recommended that the seal cavity be thoroughly flushed with DI water.

SIP

It is recommended that SIP be performed while the shaft is stationary. The goal of SIP is to heat soak the equipment to a target time and temperature. If a flow of cool lubricating water is provided to the seal the goal of the SIP will be defeated in and around the seal. Conversely if the lubricating barrier fluid water is allowed to heat to the soak temperature, it would have greatly reduced lubricating properties and the seal would be damaged.

The sterilization process can be the most difficult process for the seal to tolerate. Unlike the CIP that is normally restricted to the vessel side of the seal, SIP may be required inside the seal cavity. The sterilization of the seal cavity prevents living organisms that may be present in the cavity from being forced into the vessel due to the higher barrier fluid pressure that exists in the dual pressurized seal.

Elastomers have a tendency to take a compression set when exposed to steam, so the proper selection of O-rings is essential. The steam has at least two purposes in and around the seal. First and foremost is the desire to raise the temperature of all surfaces, cracks, and crevices to a target temperature to kill all living organisms. Secondly, and often not a consideration, is the sweeping action steam can have as it moves through a chamber or cavity. If the removal of debris is required this may be done by a CIP process.

A target time and temperature have been selected for sterilization, usually 131°C (267.8°F) for an hour or so. If all the components of the seal, including cracks and crevices arrive at the target temperature then it can be assumed that the level of sterilization desired has been acquired. Time must be allowed for the temperature to penetrate all areas and it is felt that after the atmosphere inside the seal chamber is stabilized at 131°C (267.8°F) that an hour exceeds any soak time requirements.

CONCLUSION

Pharmaceutical and biotech industries provide specific challenges for mechanical seal design and system selection. These challenges continue to evolve as new processes are developed. While there are differences between these two industries, there are also many similarities. There is no one seal design that is suitable for all applications. Specific material selection and design features must be closely examined for each application. Fortunately, there is a large experience base of applications running in these industries that provide a guide to sealing most applications. As with any application, though, successful sealing can only occur if there is a complete understanding of the process conditions, equipment condition, and the cleaning/sterilization requirements.