Tech Talk

Improvements in Installation Practices of Bioprocess Piping Systems

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Installation practices at modern biopharmaceutical, pharmaceutical and some food and dairy plants today are quite different than those at similar construction sites 20 years ago. The specification for the use of machine or orbital GTA welding together with the development of the ASME Bioprocessing Equipment (BPE) Standard has resulted in cleaner, more repeatable welding of piping and components such that thousands of welds are routinely installed with very low reject rates. Today's improvements in hygienic design and cleanability of process piping systems are considered essential for the production of bioengineered pharmaceutical products.

The ASME Bioprocessing Equipment (BPE) Standard [ref 1]

Problems with defective welds on process equipment imported from Europe was the initial catalyst that led to work on the BPE Standard. In 1988 an engineer at a biotechnology plant in San Francisco, California was preparing to install some process equipment and recognized that the welds on the equipment were of insufficient quality to meet the stringent hygienic requirements necessary for growing cells in culture. Since existing standards were insufficient for this new technology, the engineer recruited a group of suppliers and end users in the industry and they approached the American Society of Mechanical Engineers (ASME) for permission to begin the writing of a new standard for the developing Bioprocess Industry. Work on the BPE was begun and the first edition was published in 1997. Revisions appeared in 2002, 2005, and 2007. A new BPE edition for 2009 was released for publication in October, 2009.

Achieving welds of consistent high quality compatible with the principles of hygienic design was an initial goal of the BPE Committee, but the Standard is by no means limited to welding and fabrication issues. The BPE Standard deals with the requirements of the bioprocessing and pharmaceutical industries, as well as other applications with relatively high levels of hygienic requirements or bioburden control. BPE covers directly or indirectly the subjects of design of process equipment for cleanability and sterility, component manufacture, materials of construction, fabrication including welding, pressure systems (vessels and piping), examinations, inspections, testing and certifications.

The BPE Standard applies only to new construction and only to those systems and components that are in direct or indirect contact with the product. It does not apply to those components that are not in contact with the finished product or part of the intermediate manufacturing stages. The BPE is an American National Standard that, by 2002, had become an adopted International Standard referenced in 29 countries. Use of the BPE Standard has continued to grow to the point that virtually all new biopharmaceutical plants in the United States and many foreign countries, have been designed to, or have retroactively incorporated its requirements into, their specification.

Orbital Welding to the BPE Standard - Improved Weld Quality and Repeatability

The stated purpose of BPE Part SD of the BPE Standard - Design for Sterility and Cleanability is "to create a design framework using proven practices, for maintaining clean and sterile process systems." From the beginning, orbital GTA welding was recommended by the BPE for joining of piping and process components. (Figure 1.) Although the repeatability of orbital welding power supplies had the potential to deliver higher productivity than manual welding because of improved weld repeatability and less need for re-work, conditions existing in the Industry at that time made the fulfillment of this promise problematic. Prior to the introduction of the BPE in 1997, there was no consistency in material chemistry or in the dimensions of weld fittings used in biopharmaceutical applications. Material chemistry is important because stainless steel shows considerable heat to heat variation in weldability so that weld parameters that produced successful welds on one heat of material would need considerable adjustment for other heats. Consistent dimensions are important as the welding current is based on wall thickness. Other dimensions affect fit-up, etc. Welds at that time were often discolored due to poor inert gas purging. These conditions were addressed by the BPE Subcommittee on Material Joining (MJSC) and the Subcommittee on Dimensions and Tolerances (DTSC).

The MJSC developed a set of weld criteria that, in addition to code criteria for adequate structural integrity, was designed to minimize the growth of microorganisms and promote cleanability. Orbital welds are smoother than manual welds and, when done properly, are free from crevices, pits and other defects that could harbor microorganisms. All welds must have complete penetration to the inside surface of the weld which, in bioprocess applications, is usually the product contact surface. Unpenetrated welds are entrapment sites for product and are difficult to clean. Process piping lines are sloped for drainability as gravity is the most efficient means of draining fluid from a system. Limits on inside diameter (ID) and outside diameter (OD) concavity and misalignment are set to promote drainability and cleanability of weld surfaces.

Control of Material Chemistry and Weld End Dimensions

Prior to the introduction of the BPE, piping and component materials in biopharmaceutical applications could be 304 or 316 or 304L or 316L stainless steel. The BPE recommended the use of 316L for weld ends but there is considerable heat-to-heat variation in the weldability of stainless steel so even when only 316L is used, variations in trace element composition, especially sulfur content can cause problems in welding. Very low sulfur material is difficult to weld since the weld pool tends to be shallow, wide and difficult to obtain uniform joint penetration. But a greater problem results when welding fittings to tubing with large differences in the sulfur content. In this case, the weld pool may shift favoring the low sulfur heat and lack of penetration may occur. While the AISI specified only an upper limit for sulfur of 0.030 wt%, BPE has specified both an upper limit of 0.017 and a lower limit of 0.005 wt.% sulfur for weld ends of fittings, valves and other components. This has virtually eliminated all of the problems related to sulfur content and greatly improved installation of biopharmaceutical systems.

In the 2009 Edition of BPE there will be a new Part CR Certification. Manufacturers of tubing and/or fittings that comply with ASME requirements for certification will be permitted to mark their products with an ASME BPE Stamp that certifies that the facilities have the capability to

manufacture compliant products and that products so marked have the specified chemical and dimensional properties and appropriate surface finish.

Discoloration

One of the contributions of the BPE Standard to achieving high quality hygienic welds was to specify the amount of color permitted on the ID of the weld and heat-affected zone (HAZ). While no color is permitted on the weld itself, a slight color may be allowed on the HAZ. As a guide, the BPE refers to the American Welding Society (AWS D18.1 and AWS D18.2) Specification for Welding of Austenitic Stainless Steel Tube and Pipe Systems in Sanitary (Hygienic) Application [ref2] which published a color photo showing the amount of weld discoloration on the ID surface of a series of orbital welds. Weld discoloration was shown to increase with increasing amounts of oxygen added to the ID (argon) purge. (Figure 3.)

This figure allows owners, installing contractors and QA people to agree in advance to the amount of weld discoloration acceptable for a particular application. Since the amount of discoloration has been shown to correspond to a loss in corrosion resistance, and the products of corrosion can result in contamination of the system, this is not just a cosmetic issue. Contaminants other than oxygen, including moisture, oil or grease on the tubing, etc. can result in weld discoloration, thus the color on the chart rather than the oxygen content of the purge gas is the acceptance criterion. Owners typically specify sample number three as the upper allowable limit, but obviously would prefer welds in the 1-2 range with minimal discoloration.

Facility Design for Improved Workflow and Efficiency

An example of how a manufacturer of bioprocessing equipment optimized their production, Sartorius BBI Systems, Inc. (SBBIS) designed and organized an entire facility to improve workflow and efficiency and to streamline procedures.[ref 3] These procedures included improved work flow for orbital welding of tubing and components in compliance with the BPE Standard (Figure 4.) In addition, the facility is arranged so that fabrication is performed in areas where the product contact surfaces are protected from contamination and surface contamination is prevented. When electropolishing of welded assemblies is specified, SBBIS does the electropolishing in-house to prevent the contamination that would result from transport to another facility. This has significantly improved the hygienic aspects of installation technology in their facility.

Reasons for Greater Percent of Orbital Welds

In the past there were many places in systems and equipment that an orbital weld head would not fit so a larger percentage of welds had to be done manually. Newer designs in weld heads such as the Arc Machines, Inc. Model 8 series, which is narower than previous designs, has led designers of equipment and piping systems to design for orbital welds and now virtually 100% of field welds in biopharmaceutical applications are done orbitally.

Inspection and Examination of Welds

Weld Inspection and Examination has become more systematic in recent years. The ASME BPE, in accordance with the ASME B31.3 Process Piping Code, makes the distinction between Examination and Inspection. B31.3 requires that the external surface of all welds be examined and a minimum of 20% of the welds be inspected internally on the product contact surface with a borescope or, when accessible, by direct visual inspection. Examination is done by the installer or the person performing the weld while inspection must be done by the owner or his representative who may be a third party QA/ QC company or consultant. The contractor must submit an inspection plan in which the percentage of welds to be inspected must be agreed upon by the owner/user, installing contractor and/or engineer. This in-process borescopic examination is done in lieu of radiography that would otherwise be required.

Test coupons or sample welds are made and evaluated pior to production welding to demonstrate that the welding equipment is working properly and that the purge is satisfactory (Figure 5.). Coupon welds are done at specified intervals throughout the project such as at the beginning of a shift, when the power supply is moved, etc. A BPE Weld Log is maintained during a project for coupon welds as well as for production welds. Each weld has a unique number and the locatiion of any weld in a facility can be traced to a particular isometric drawing creating a weld map (Figure 6.) For each weld there is a record of the date it was welded, the welding operator's ID number, and whether the weld was examined or inspected. Any component welded into the system is identifiable and the materials from which it was fabricated can be traced back to the mill.

Welding Documentation

Welding documentation includes documents certifying the welding procedures and welding personnel to ASME Sect. IX of the Boiler and Pressure Vessel code which consist of Welding Procedure Specifications (WPSs), Procedure Qualification Records (PQRs), and Welder Performance Qualifications (WPQs) for manual welders, and Welding Operator Performance Qualifications (WOPQs) for orbital welding operators. The Qualifications for Inspectors and Examiners must also be included.

Equipment Installation

Installation of equipment in biopharmaceutical applications have been made more efficient by the use of skid-mounted equipment modules so that installation and fabrication can be telescoped into a shorter timescale. Fabrication and in some cases installation and commissioning of the skids can occur at the same time as plant construction. This means that all of the materials and components must be inspected prior to installation and provision for weld inspection and documentation must happen during the manufacture of the skid. For the recent expansion at Lonza Biologics Expansion in Singapore, process equipment for the large scale mammalian biopharmaceutical production plant was fabricated, tested and disassembled in the United States, and then shipped to Singapore for reassemblyonsite. Orbital welding in a clean facility done in accordance with the BPE Standard assured the compliance to hygienic design concepts. (Figure 1.)

Passivation Procedure Qualification

Field welds in hygienic piping systems are typically left in the as-welded condition; the only post weld treatment being chemical passivation with nitric or citric acid solutions following installation. Passivation restores, at least in part elements in the passive surface layer that are disturbed by welding and the concomitant loss of corrosion resistance. The BPE Surface Finish Subcommittee has added a new non-mandatory appendix to the 2009 Edition of BPE that offers guidelines to owners for qualification of their passivation procedures.

Living Standard

The BPE Standard is a consensus standard with work done by volunteers. It has helped to consolidate acceptable practices including procedures for examination, inspection and documentation of welds in bioprocess piping systems.

While the BPE Standard specifies what the end result must be, it does not provide guidelines for installers telling them how to achieve the desired results. Installation practices (SOPs) developed by installing contractors are written procedures that all welding and installation personnel must follow. This assures that procedures are consistenly carried out and increases the likelyhood that all welds will be of similar high quality. The contractors' SOPs become part of the Turnover Package submitted for validation of the project. Not sure if this needs a paragraph or for the two lines to be moved together.
Standards such as BPE operate on the assumption that quality must be built in - it cannot be added after the fact. The Standard is continuosly being updated to represent a consensus of current good manufacturing practices (cGMP) for the biopharmaceutical industry.

Summary

The last 20 years have seen dramatic improvements in fabrication technology. Orbital welding has been central to this advancement while standardization of weld end dimensions and chemistry by the BPE have resulted in more repeatable welding procedures. The BPE Committee has reached its initial goal of achieving welds of consistent high quality compatible with the principles of hygienic design.

References

1. ASME Bioprocessing Equipment (BPE) Standard. American Society of Mechanical Engineers. New York, NY. http//cstools.asme.org

2. AWS D18.2 Guide to Weld Discoloration Levels on the Inside of Austenitic Stainless Steel Tube. American Welding Society (AWS) Miami, FL: www.aws.org

3. Stadler, Henon and Koiro. Designing a CGMP Equipment Manufacturing Facility. BioProcess International, June 2007

Photo Captions:

Figure 1. An orbital welding operator welding a tubing assembly at a biotechnology expansion in Singapore. *Photo courtesy of Kenyon Engineering.*

Figure 2. A good machined end-preparation is important for fit-up of the weld joint and for achieving repeatable orbital welds. *Photo courtesy of Arc Machines, Inc.*

Figure 3. Color chart from AWS D18.1/D18.2. Weld discoloration relative to amounts of oxygen added to ID purge gas. *Photo courtesy of American Welding Society.*

Figure 4. Arc Machines Model 207 power supplies and Model 8 weld heads used in the manufacture of bioreactors and fermentors. *Photo courtesy of Sartorius BBI Systems, Inc. and Arc Machines, Inc.*

Figure 5. Orbital weld cut open for inspection of the ID surface. Weld coupons or test welds are routinely used for Quality Assurance of biopharmaceutical process piping systems. *Photo courtesy of Protech Process, Inc. and Arc Machines, Inc.*

Figure 6. An orbitally welded assembly for a CIP pump for a 750-l fermentor. The location of the assembly is shown on the weld map with the position of each weld numbered. The yellow control document travels with the part as it is fabricated. *Photo courtesy of Sartorius BBI Systems, Inc.*

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Dr. Henon joined the ASME BPE Standards Committee in 1989 and served for two terms as Vice Chair of the Main Committee. She is currently a member of the BPE Materials Joining and Surface Finishes subcommittees and the Subcommittee on General Requirements. She is the official Liaison between the ASME BPE and ASME B31.3 Process Piping Committee which is currently writing a High-Purity chapter. She also serves on the American Welding Society (AWS) D10 Committees and AWS D18 Committees.

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