



Without harmonization between the various [American National Standards] Developers the usefulness of industry Standards would most likely be diminished by conflicting requirements and overlapping stipulations.

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Across the wide spectrum of the more than 200 American National Standard (ANS) Developers, those organizations accredited by ANSI (American National Standards Institute) to develop industry Standards, and the more than 10,000 American National Standards that are published by those ANS developers, there is an ongoing and dynamic effort to ensure harmonization among the many Standards.

Two ANS developers that directly impact the pharmaceutical industry are the American Society of Mechanical Engineers (ASME) and ASTM International, formerly known as the American Society for Testing and Materials (ASTM). As a result of this harmonization effort the engineer of an API (Active Pharmaceutical Ingredients) facility can readily make use of multiple Industry Standards on a single project without concern of conflicting statements between those Standards. That is not to say that a more stringent requirement will not exist in one Standard over another. This is normally rectified by including, in proprietary specifications and guidelines, a statement to the effect that, “the more stringent requirement shall govern”.

In adopting industry Standards, such as those published by ASME and ASTM, an engineer is drawing upon the consensus of committees of experts in which the results of pertinent subject matter have been assessed, analyzed, debated, and voted on at multiple levels, culminating in accredited standardization. Not only is the content of these industry Standards arrived at through a rigid internal process, but also through inter-standard communication.

What this means for the end user is this: Unless a project is regulated by a specific Code that has been adopted as a Federal, State, or municipal regulation, you may specify, through contract stipulation or project specifications, the requirement to comply with a particular set of Codes and Standards. These requirements may specify, as an example, ASME B31.3 – Process Piping as the main compliance piping Code for a project, with or without exceptions. Additionally, the project requirements will dictate the need to reference Codes and Standards beyond those requirements captured in B31.3.

Such requirements will include Standards for components and material of construction (MOC), as well as specialized needs such as those carried in the ASME – BPE (Bioprocessing Equipment) Standard. In the case of the component related Standards, these are generally adopted as a whole with optional requirements within the particular Standard that need to be specified in the procurement documentation. The same holds true with material Standards published by ASTM. These Standards too are adopted as a whole with optional requirements within the Standard that need to be specified in the procurement documentation.

When using a piping Code such as B31.3 as a base Code for a project other piping Codes and Standards can be referenced for compliance when the following occurs:

1. The referenced requirement is not already contained in the base Code,
2. The referenced requirement is more stringent than that contained in the base Code,

3. The referenced requirement does not conflict with a “not permitted” statement in the base Code. Such as:
- a. B31.3 Para. 306.4.4(c) *A flared lap is **not permitted** under severe cyclic conditions.*

This discussion thus far leads me to make the point that even though a project has adopted a base piping code,

of the possible piping Codes and Standards needed for an API type project and how they overlap and comingle within the framework of a project, or within the infrastructure of plant operations and maintenance. In actuality this graphic would be a great deal more complex due to the sheer volume of Codes and Standards a project or plant operations would require.

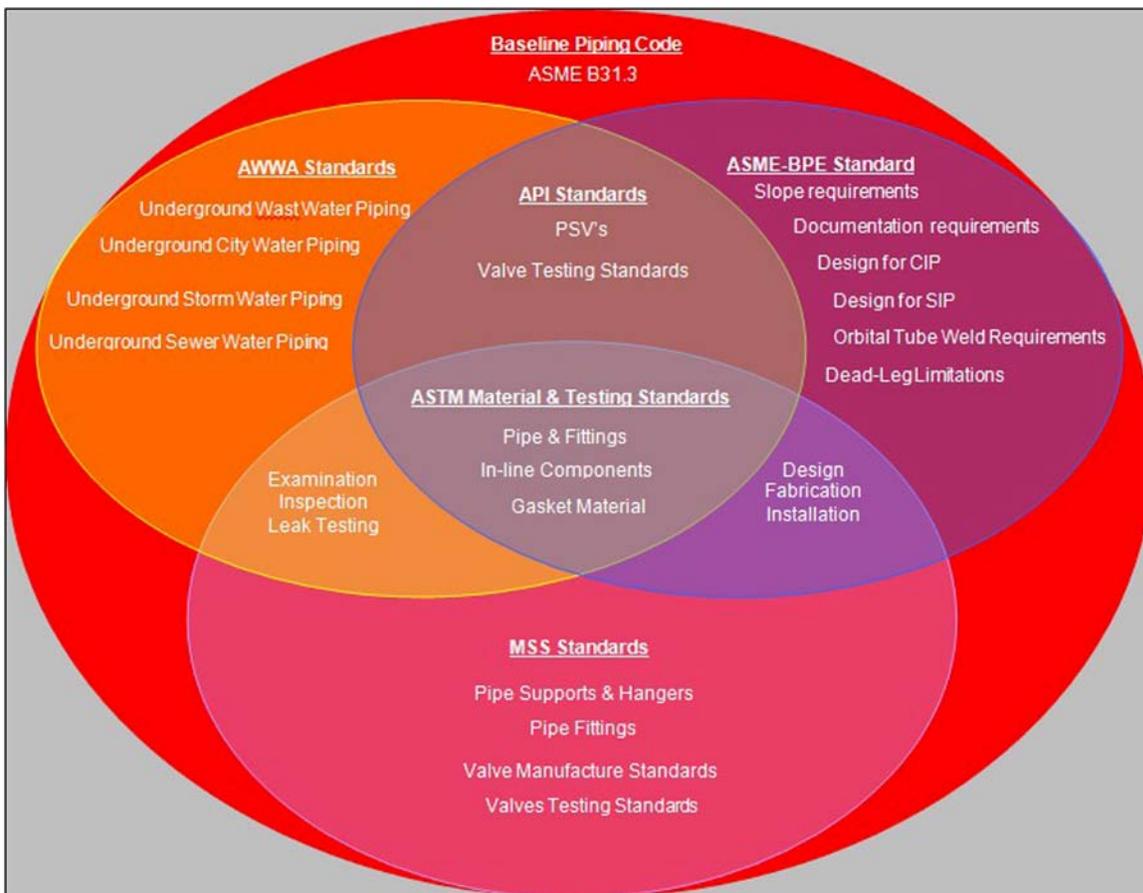


Figure 1 – Venn Diagram of codes & standards requirements

either by the authority of government regulation or by engineering decision, it is beneficial and even necessary for the engineer to look to other Standards in defining additional requirements a project will need beyond those covered in the base code. Rather than a company spending time and money defining needed requirements not covered by B31.3, as an example, look to other standards in which vetted requirements matching a project’s needs may already exist.

What a project’s Codes & Standards requirements may look like graphically is represented in the rather simplistic Venn diagram of Fig. 1. What this shows is a basic representation

ASTM – Working with the Pharmaceutical Industry

A key factor in achieving hygienic conditions for manufacturing pharmaceutical grade products is in the material that comes into direct or indirect contact with the product. The workhorse material in this industry is 316L stainless steel under the ASTM Standard A270-S2.

Because the welders and welding operators performing circumferential butt welds for hygienic piping are required to make acceptable autogenous welds (welds without filler metal) on a repeatable basis under closer tolerances and additional scrutiny than general piping requires, the majority of those welds are accomplished with semi-

automated welding machines called orbital welders. Achieving repeatability with orbital welders requires that the material of the two components to be welded have very similar chemistries; in particular their sulfur content.

Until as recently as the mid 1990's engineers designing a pharmaceutical grade facility had to specify, and fabricators had to match, heat numbers on tubing and components that were to be welded together. This time consuming exercise in specifying, locating, ordering, verifying, and stocking tubing and components with these matching heat numbers was, at times, a logistical nightmare; not to mention the added cost in performing this effort. The heat number itself is a tracking number for metallic material that allows the material to be traced back to its original chemical composition at the time of its formulation in the mill.

Documentation, in the form of Material Test Reports (MTR's), is one part of the rigid documentation records required when building a pharmaceutical manufacturing facility. The MTR provides certification of the chemical composition of the material along with the heat number to validate that data. The reason for going to all the trouble of matching up heat numbers was instigated by the need to match up compatible sulfur content within the material composition. That information is included in the MTR.

Without getting too far off topic, the amount of sulfur content in the metal affects the weld pool. A high level of sulfur (sulfur having a high electron affinity) instigates a restricted anode spot at the weld providing excellent penetration. Lower sulfur content instigates a diffuse anode spot at the weld causing less penetration and a wider weld pool. When two components, having the same, or similar sulfur content are welded together the weld pool will form equally on both pieces allowing the weld pool to flow evenly about the predetermined path of the orbital welder's tungsten electrode. Should the sulfur content of the two components vary significantly, the weld pool will have a tendency to flow unevenly about the predetermined path of the orbital welder's tungsten electrode, possibly creating lack of fusion and an unqualified weld.

As an example of harmonization between ANS developers, ASTM, in response to the needs of the pharmaceutical industry as requested by ASME-BPE, created the supplemental S2 under A270, written as A270-S2. The S2 supplement stipulates a much narrower range for the sulfur content in A270 abating the need for having to match up heat numbers. The more suitable sulfur range requirement of 0.005 to 0.017%, rather than the normal max limit of

0.030%, placed all A270-S2 stainless steel, no matter the heat, within a compatible range for orbital welding. This alleviated the costly and time-consuming need to match heat numbers of tubing and components that required welding.

ASTM, under A380 and A967, also provides the basis for needed protocols in the cleaning and Passivation of piping systems. Also included in A380 and A967 are protocols for surface testing stainless steel to ensure sufficient Passivation of the material's surface. These are essential elements in establishing and maintaining a system of pipe and equipment for pharmaceutical processing.

In its 2009 publication the ASME-Bioprocessing Equipment (BPE) Standard makes reference to these ASTM protocols in its Non-Mandatory Appendixes. In Appendix E of the BPE Standard it provides a "Test Matrix for the Evaluation of Cleaned and/or Passivated Surfaces". The matrix not only provides a listing of pass/fail testing protocols taken from ASTM A380 and A967, it also lists suggested cutting edge testing to determine the chemical composition of the tubing material's surface. These cutting edge tests can determine, not only the quality of the chromium rich passive layer, but also its depth, providing a qualitative analysis not simply a pass/fail result.

The ASME-BPE Standard

The conceptual intent, the basis for what drove a group of engineers in the late 1980's to petition the ASME Council on Codes and Standards for the approval to create what is now titled the ASME-Bioprocessing Equipment (BPE) Standard, was the real need and necessity to inject some sense of continuity and standardization into an industry that sorely needed it — the pharmaceutical industry. This Standard has proven to be a salient part of the continued growth and refinement of that industry. As technology and regulations evolve the BPE Standard will continue to keep pace.

The BPE Standard, first issued in 1997, dovetails nicely with the ASME B31.3 Process Piping Code, the essential piping Code for industry in general. The initial BPE Standard consisted of six Parts, which included:

- Part GR – General Requirements
- Part SD – Design for Sterility and Cleanability
- Part DT – Dimensions and Tolerances for Stainless Steel Automatic Welding and Hygienic Clamp Tube Fittings

- Part MJ – Material Joining
- Part SF – Stainless Steel and Higher Alloy Surface Finishes
- Part SG – Equipment Seals

The latest version of the BPE Standard, which at this writing is the 2009 issue, looks much different than its inaugural predecessor with content that is much more encompassing and broad-ranging with three additional subject matter sections referred to as Parts. Those additional parts include:

- Part PM – Polymer-Based Material (Added in 2002 issue)
- Part MMOC – Metallic Materials of Construction (Added in 2009 issue)
- Part CR – Certification (Added in 2009 issue)

In the next issue of the BPE, which is scheduled for 2012, there will be an additional Part added for Process Instrumentation, Part PI. This new Part will cover requirements for design, installation, and application of Process Instrumentation. Referring to process in this context also includes utility fluids such as purified water, water for injection (WFI), clean steam and other utilities which come in contact either directly with the product or indirectly through contact with the product contact surface during cleaning or sanitization.

At the core of the BPE Standard is the need to install piping systems and equipment that will become and will remain hygienically clean by making them drainable and cleanable, to a microscopic level. Residual hold-up of product, a system that cannot be properly cleaned or sterilized in place, or a system that facilitates the onset and growth of bioburden (a colony of microorganisms) cannot be tolerated in pharmaceutical piping systems.

The CIP process is a procedure by which a cleaning solution is pumped through a piping system at scheduled intervals to kill and clean out targeted bacteria and process residue. The SIP process performs essentially the same procedure using steam with the intent to sterilize the system. Both of these procedures are essential elements in the hygienic production of pharmaceutical products. In saying that, it is also essential that these augmented systems be designed to integrate properly with the process and product piping systems.

In designing a process system that requires CIP or SIP there are specific piping and equipment design requirements that need to be met. Requirements such as minimum slope, maximum dead-leg, internal weld finish, fitting and fabrication tolerances, surface finishes, etc. are all necessary to accommodate those procedures. By not understanding the need for these requirements, and therefore not integrating them properly into the design of a system that requires CIP or SIP, the goal of cleaning or sterilization will not be met. All of those requirements necessary for this type of design can be found in the BPE Standard.

Specifying the proper material of construction, design attributes, fabrication criteria, installation requirements, examination and testing protocols at the frontend engineering effort is essential. However, it is critical that adherence to these requirements be verified throughout the life-cycle of a project through proper documentation. The laundry list of documentation specified in the BPE Standard is one that can be utilized simply by reference. And this is where the real benefit of industry Standardization becomes apparent. Rather than writing out a requirement that may already exist in an industry Standard simply reference the respective paragraph in a Standard containing the needed requirement.

Content of the BPE Standard

As eluded to earlier, while the BPE Standard dovetails with and references many aspects of B31.3 it is markedly different in both layout and content. You will see, as we touch on a few key elements of the nine current Parts of the BPE Standard, how universal the Standard actually is.

PART GR

The General Requirements section of the Standard sets the tone and defines the scope of the Standard. This section provides definitions for terminology that may be specific to the bioprocessing industry, or it could be a term used elsewhere, but with different implications in the BPE Standard. Terminology defined elsewhere and adopted by the BPE Standard under that definition, will have the definition referenced rather than re-written or paraphrased in the BPE Standard.

PART SD

The section on Design for Sterility and Cleanability is one aspect of the BPE which departs from the main focus of the B31.3 format. Whereas, B31.3 is developed around the cornerstone of safety and system integrity, it is necessary for the BPE to broaden its content to also include

acceptable criteria for system design as well as safety and system integrity.

In doing so, the SD subcommittee, since its inception, has taken on the task of researching industry design practices used both currently and in the past in the bioprocessing industry. This is an effort to validate and, where necessary, rectify those largely unqualified design practices and criteria, while at the same time developing new and appropriate design criteria for adoption into the BPE Standard.

Some of the topics covered by PART SD are clear concepts on how to design cleanability and Sterility into a system. It also covers specific design issues with regard to instrumentation, hose assemblies, filtration and other equipment. In addition to hydrostatic testing it also touches on testing fundamentals for spray balls, drainability, cleanability, and sterility. There is also a listing of documentation that can be selected by and for industries beyond that of bioprocessing.

PART DT

The Dimensions and Tolerances section has basically standardized tubing, components, and equipment used in the bioprocessing industry. Prior to the BPE and PART DT there were no Standard dimensions on fittings and valves. Nor were there a common set of manufacturing tolerances. This meant that components from one manufacturer to the next were not necessarily interchangeable. This presented a logistical nightmare for a project in which all fittings had to be purchased from the same manufacture to ensure compatibility and fit-up.

PART MJ

The Material Joining section touches on all aspects of the welding of pressure vessels, tanks, tube, and fittings. It takes the reader from acceptable material requirements through inspection, examination, and testing requirements. In between it discusses such topics as joining processes and procedures, weld joint design and preparation, weld acceptance criteria, procedure and performance qualification, and documentation requirements. Included are Tables listing weld acceptance criteria and detail graphics on acceptable/unacceptable welds.

PART SF

One of the necessary attributes in obtaining and maintaining a clean system is in the quality of the product contact Surface Finish. Whether in the bioprocessing industry or other industries in which at least a segment of

the processing scheme is biological, such as the biofuel industry, the cleanability of the product contact surface is crucial to the efficiency and effectiveness of the process itself. Not only has PART SF brought to the pharmaceutical industry methods by which surface finishes are classified, it also provides acceptance criteria with which manufacturers or service providers can be required to comply with.

PART SG

PART SG covers various types of mechanical seals. In so doing, this Part has provided seal classifications describing the required integrity of a seal under specific service conditions.

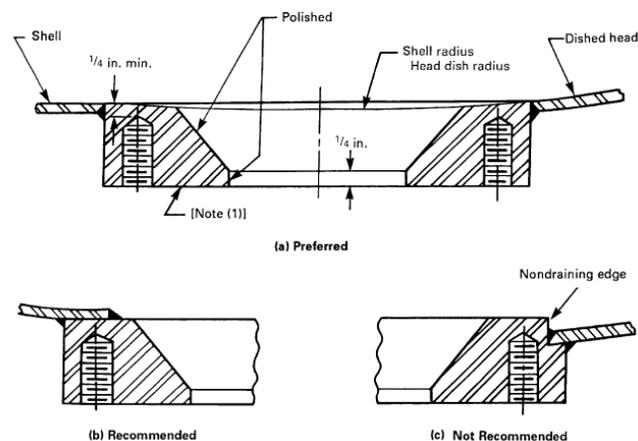


Figure 2 – Side and Bottom Nozzle Pads

PART PM

This section on Polymer-Based Material includes both thermoplastics and thermosetting materials. It touches on design considerations, joining methods, interior product contact surfaces, requirements particular to those for single-use components and equipment, hose assembly requirements, and materials of construction.

PART MMOC

The section on Metallic Materials of Construction was first published in the 2009 issue of the BPE Standard. Its incorporation into the Standard was driven by the need to keep abreast of industry's continuing search for alternative materials of construction (MOC), beyond that of 316L stainless steel. The main objective of Part MMOC is to improve system quality and sustainability as well as improve compatibility for fluids too aggressive for 316L.

Adding PART MMOC allowed the Standard to elaborate and expand its information on metallic material in a way that would otherwise have been too segmented and convoluted. As it turns out, this section on metallic materials provides,

not only a definitive listing of acceptable material in its various forms, but also provides such information as PREn (Pitting Resistance Equivalent Number) Rankings, Corrosion Test references for Alloys, discussion points on Superaustenitics, duplex stainless steels, nickel alloys, ferrite content restrictions, and much more. Information that helps support the reader's effort in seeking out appropriate materials of construction (MOC)

PART CR

PART CR was first included in the 2009 issue as a means of providing a program that would assure end users that tubing and fittings they purchase are compliant with the BPE. This is accomplished through a well defined and implemented certification program for compliance of the BPE Standard by those manufactures, fabricators, and service providers who qualify. The certification process is a

FIGURES, TABLES AND NON-MANDATORY APPENDIXES

The BPE Standard is loaded with over 60 Figures, 60 Tables, and 9 Non-Mandatory Appendixes, all in an effort to make very clear what it is the user needs to comply with. The Figures graphically represent everything from fitting dimensions to mechanical seals. It also includes acceptable nozzle projections, side and bottom nozzle pads (Ref Fig. 2), vessel sight glass mounting design (Ref. Fig. 3), double mechanical cartridge seal design (Ref. Fig. 4), weld profiles, design diagrams, and much more.

In addition to the many Tables on dimensions and tolerances for the manufacture of fittings there are tables that include such information as Weld Acceptance Criteria for: welds on Pressure Vessels and Tanks; welds on Pipe; welds on Tubing; and Tube Attachment Welds. There is also a Table for Acceptance Criteria for Stainless Steel and

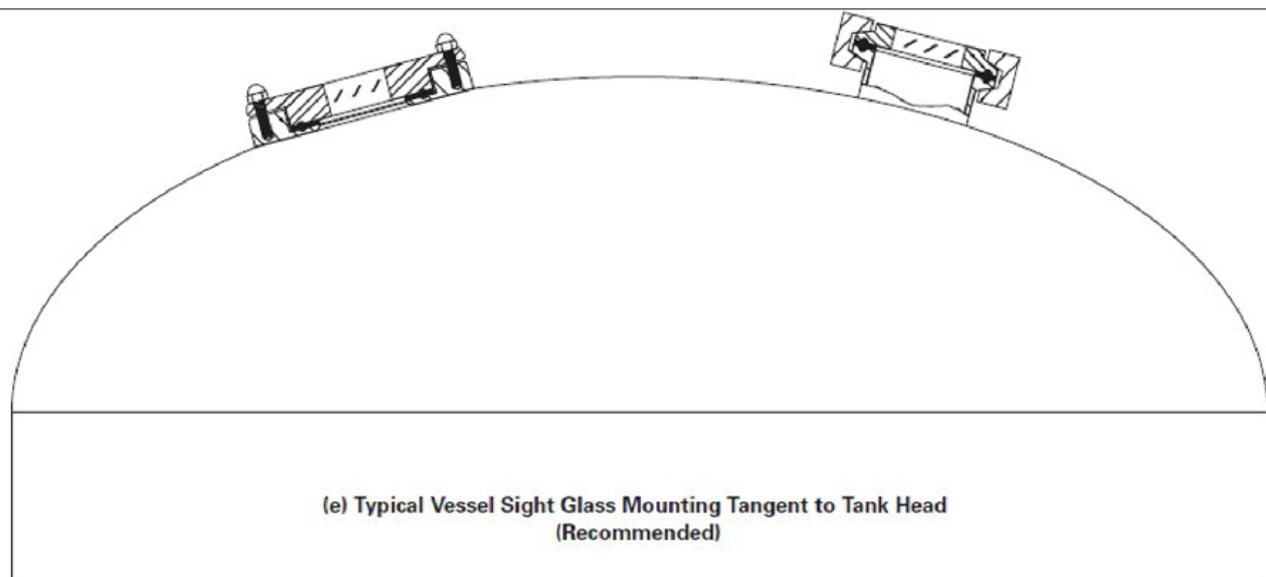


Figure 3 – Sight Glass Mounting

multi-faceted program based on an in-depth Quality Management System (QMS) as defined in PART CR.

The program requires that the applicant for certification create a QMS manual, as defined in the BPE Standard, which is expected to mirror the quality program actually being used in their production process. Among many other requirements, the manual should reflect a company's organizational hierarchy, inspection protocol, material handling procedures (from receiving through manufacturing and shipping), segregation of materials, inspection personnel qualification, reject resolution, documentation, and much more.

Higher Alloy Mechanically Polished Product Contact Surface (Ref. Fig. 6), and a Table of Surface Finish Designations (Ref. Fig. 7).

The Tables, Graphics, and intellectual information that end up in the BPE Standard are the product of a very structured data refining process. The information that makes it into the BPE Standard is typically distilled from a much larger data source compiled over time as a result of research performed or directed by personnel within its membership, who, I might add, very often absorb the time and expense in executing this research. A great deal of that research information is very useful, but cannot be considered as suitable for the body of the Standard.

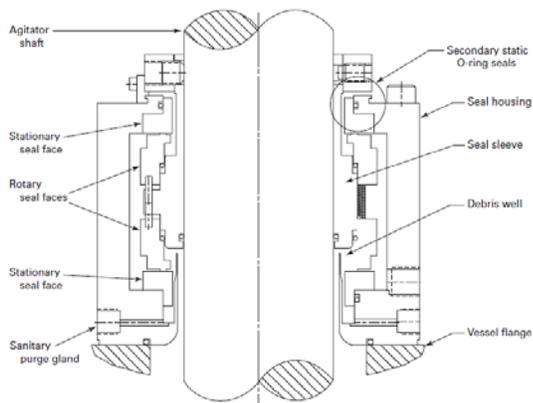


Figure 4 – Double Mechanical Cartridge Seal

Not wanting this useful information to end up residing in a file box or to sit idly on a hard drive, and therefore not get shared with industry, the BPE has added a Section for Non-Mandatory Appendixes. This is a section of the Standard in which information, deemed useful to readers of the Standard, but not appropriate for codification, can be posted for use while remaining segregated from the requirements of the Standard should the entire Standard be adopted as Code.

The Non-Mandatory Appendixes covers such topics as:

- Appendix A – Slag
- Appendix B – Material Examination Log & Weld Log
- Appendix C – Slope Measurement
- Appendix D – Rouge and Stainless Steel
- Appendix E – Passivation Procedure Qualification
- Appendix F – Corrosion Testing
- Appendix G – Ferrite
- Appendix H – Electropolishing Procedure Qualification
- Appendix I – Vendor Documentation Requirements for New Instruments

And Finally

What you hopefully take away from this article is not just a cursory understanding of the BPE Standard, but also the understanding that there is a great deal of useful, vetted information at your fingertips in the form of American National Standards. While some Standards may require compliance from a regulatory standpoint others are yours to adopt and specify as you need. And as stated previously, it is not necessary to adopt an entire Standard if all you need are isolated references.

As an example, if all you need from the BPE Standard is some or all of its content on CIP requirements then reference that segment of the Standard. Only that

referenced segment of the Standard becomes contractual for your project or facility. The same thing holds true if your project is handling, let’s just say, hydrogen gas. There may be circumstances in which it may be practical to specify compliance with isolated segments of a Compressed Gas Association (CGA) Standard such as G-5 “Hydrogen” and/or G-5.4 “Standard for Hydrogen Piping Systems at Consumer Locations.” If so, then simply adopt and reference that segment of the Standard.

There is a diverse number of Standards Developers (ASME, BPE, CGA, etc.) required to deliver the necessary specifications and guidelines to a project. Without harmonization, as mentioned earlier, between the various Developers the usefulness of industry Standards would most likely be diminished by conflicting requirements and overlapping stipulations. However, with harmonization and self familiarization of these Standards our work of selecting and employing the many available Standards is made much easier and more relevant. ■

Acknowledgements:

1. Henon, B. K., “Orbital Welding of Stainless Steel Tubing for Biopharmaceutical, Food and Dairy Applications”, published in Tube International, September, 1999.
2. Henon, B. K., “An Overview of the Effects of Sulfur on the Orbital GTA Welding of AISI Type 316L Stainless Steel Tubing and Pipe”, presented at a SEMI Workshop on Stainless Steel at Semicon SW, Austin, Texas, October, 2000.

References:

1. American Society of Mechanical Engineers (ASME)-Bioprocessing Equipment (BPE) Standard 2009 Edition.
2. American Society of Mechanical Engineers (ASME)-B31-1 Power Piping 2007 Edition.
3. American Society of Mechanical Engineers (ASME)-B31.3 Process piping 2008 Edition.
4. ASTM A270-03a.

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W. M. (Bill) Huitt has been involved in industrial piping design, engineering, and construction since 1965. Positions have included design engineer, piping design instructor, project engineer, project supervisor, piping department supervisor, engineering manager and president of W. M. Huitt Co. a piping

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