FEATURE FOCUS: *Bioprocessing*

getting a new life

Bioprocessing has opened a world of its own, and a standards committee is going after it.

by Alan S. Brown, Associate Editor

It isn't easy becoming a global standard. You have to work to get there.

International standards, those accepted by industry or governments in numerous countries, are issued by various organizations, from ASME to the International Standards Organization.

ASME's Boiler and Pressure Vessel Code, for example, is recognized in more than 100 countries. Of course, that code has old roots, tracing its origins to discussions among the founding members of the Society. Now, a much younger standards committee has revamped the way it does business in order to make sure its message embraces Europe and Asia.

That committee's standards address bioprocessing, the use of living organisms to create products. ASME's Bioprocessing Equipment Standards Committee attempts to define a minimum set of engineering practices that will ensure the safety and reliability of bioprocessing systems. For instance, no one wants living organisms contaminated in reactors or microbes leaking into the environment.

Bioprocessing equipment standards address a need that became apparent in the late 1980s. Genetic engineering had evolved rapidly from a laboratory procedure to a commercial technique, but the industry's equipment had failed to keep pace. Indeed, much of the hardware in use at that time was adapted from dairy equipment. So the committee took shape.

"We have only 20 years of real biotech experience," said Jay Ashrey, chair of the Design for Sterility and Cleaning Subcommittee. "We've tried to fill the code with as much information as we can, but we're still figuring it out." Ashrey is also a partner in LifeTek Solutions Inc. of Plymouth Meeting, Pa.

Bioprocessing, like most lines of business, has become a global enterprise. Its products and the equipment that make them are sold across oceans. In an attempt to grow with the field, the ASME committee is adapting its procedures to make it easier for its standards to cross borders.

One of the first moves in that direction came in May 2003, when the committee held a conference in Cork, Ireland, its first outside the United States.

"The Europeans came loaded for bear," according to Anthony P. Cirillo, the longtime chair of the BPE Committee. Cirillo is director of operations for FST Biopharm Services Inc. of Gilbert, Ariz.

At the time, more than 28 countries recognized the BPE Committee's standard. Yet most European engineers worked with competing standards published by the Deutsche International Norm, British Standards Institution, and European Committee for Standardization.

By inviting European participation, the committee hoped to bridge the gaps between competing documents and give ASME's standard a wider scope as an international benchmark. Companies could then use it to simplify the design, specification, manufacture, installation, and inspection of bioprocessing equipment and facilities around the world.

The Europeans at Cork were skeptical. "I remember looking out at the audience," Cirillo said. "They were sitting there with their arms crossed, probably wondering what the Yanks were going to try to shove down their throat this time."

Warming Up

Despite the initial coolness, the meeting in Cork proved a milestone for BPE and ASME as well. Cirillo said the committee resorted to a simple strategy to overcome Europe's frosty reception: Members listened. "We told them we were in Cork to make sure we heard their methods and philosophies," Cirillo said. "Many of them got excited about the possibilities and signed up for BPE's newly formed European subcommittee."

Its goal was to introduce European design, installation methods, philosophies, terms, and definitions into an international standard. The move was so successful, the BPE Committee eventually abolished the subcommittee title and seated Europeans on its other subcommittees.

Even though most Europeans speak English, Americans at meetings tend to talk fast and use slang, which is not always intelligible to anyone from outside the United States. So a buddy system paired individual Europeans with American committee members.

The American buddy does not interpret or translate, but instead keeps the European from losing the thread of the meeting. Europeans are encouraged to raise their hands and ask the committee to go back and explain points.

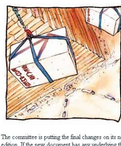
The committee is now seeking to boost Asian participation. While Asians have attended meetings for years, the committee is currently recruiting them more systematically. "We're looking outside the United States at organizations that want to become part of the BPE standard process but for language and travel reasons cannot send large delegations to meetings," Cirillo said.

Asian organizations can send individual delegates who will have the same voting rights as any other member. Those delegates will funnel information back to their organizations at home. While the Asian delegation may appear small, it will undoubtedly make itself heard because BPE is a consensus standard. That means the committee adopts only those standards upon which all members agree. The gives every individual—and every organizational representative—a significant say on any new document.

In any case, Cirillo expects Asian participation to swell. "My goal," he said, "is to reach a critical mass and have Asians participate on BPE subcommittees the same way Europeans now do. We haven't defined how this will happen yet, but we want to be proactive about getting international help."

(An article, "Culture Clash," beginning on page 36, looks at other responses to globalization, including ASME's participation in a consortium to promote American codes and standards in China.)

The committee released the first BPE standard in October 1997 and a second edition in 2002. Like most new committees, it initially focused on a handful of important areas and kept guidance to a minimum in order to reach a consensus.



The committee is putting the final changes on its new 2005 edition. If the new document has any underlying themes, they are probably measurability and consistency. According to Ashrey of the Design for Sterility and Cleaning Subcommittee, "We have to go from what we think is correct to more quantifiable design ideas. If we want to move from a standard to a code, we can't have a bunch of loose, unmeasurable items."

A standard becomes a code when it is adopted by governments or by other authorities having jurisdiction. Ashrey also wants to simplify taking measurements. "If we provide a tolerance, it should be something you can measure with a pair of calipers," he said. "Anyone can own a pair of calipers. We're trying to get away from specialized equipment."

Expect greater consistency among different sections. According to Michelle Gonzalez, principal corporate engineer at Amgen Inc. in Thousand Oaks, Calif., "We're tightening and harmonizing the different tables. If we call for a specific surface finish on a vessel, we'll use it for all tubing and fittings that go with the vessel so we don't have a hodgepodge of finishes within the same system." Gonzalez also chairs the Surface Finishes Subcommittee.

The most comprehensive changes in the 2005 edition fall under Design for Sterility and Cleaning. Its compressed water section includes more detail and graphics on ways through proper design to minimize microbial growth in highly purified water handling systems. Standards for transfer panels now include measurable tolerances for nozzle and line connections to avoid irregularities where trapped process fluids can support bacterial growth. The section also contains revised standards for fabricating hygienic heat exchangers and designing easy-to-clean piping dead legs.

BPE-2005 will also introduce a new section on polymers and elastomers. "We've defined most of the polymers and elastomers used for seals and piping," said Ted Hutton, a senior business development engineer at plastics maker Arkema Inc. in Wernson, Colo. The subcommittee has also begun to define purity and reactivity requirements for new materials and to look at disposable products.

Going Formed

The committee is looking at bigger changes in the 2007 edition, reflecting emerging technologies and the influence of international members.

For example, the BPE Committee formed a new Metallic Materials of Construction Subcommittee to expand the range of metals in bioprocessing equipment standards. In the past, virtually all standards in the field were written for 316L stainless steel, the U.S. pharmaceutical industry's standard grade. The new section will include more exotic stainless steel alloys, dual-phase steels, and superalloys. Europe has led the way with many of these materials, and has standardized on a different grade of stainless steel that provides greater corrosion resistance but is harder to weld.

BPE will seek to incorporate some of these materials into its guidelines, according to the subcommittee's chair, Ken Kimbrel, a business development manager at metal tube supplier Central States Industrial Equipment & Service Inc. in Springfield, Mo. He also hopes to set minimum alloy requirements. "Our buffer solutions and processes are growing more aggressive, but steel mills have shared their alloying elements to the lowest end of their specifications so alloys don't hold up like they used to," Kimbrel said. Setting alloying standards could help solve the problem.

Adding new metals will force changes in the Material Joining section. "You can't necessarily treat these new alloys like stainless steel," said subcommittee chair Chris Trunnell, a welding engineering manager at processing equipment maker Paul Mueller Co. in Springfield, Mo.

"When you look at stainless, the welds are bright and shiny. They almost look chrome-plated. Nickel alloys look dull and produce some surface artifacts. They don't look like good pharmaceutical industry welds, but they are. We have to educate our industry, and some of this is so new, we're still learning it ourselves," he said.

The Bioprocessing Equipment Standards Committee is running hard to keep up with the needs of its fast-changing industry. In only a few years, it has come a long way in both the depth of its standards and participation of engineers from around the world. BPE may not yet have the standing of ASME's venerable Boiler Code, but it is certainly heading in that direction.

a milk derivative

It sounds funny at first, but then it makes sense. Bioprocessing equipment grew out of the milk business.

"If you were an engineer and developed sanitary vessel specifications prior to the '30s, you probably bought your products from a manufacturer in Wisconsin," said Anthony P. Cirillo, the longtime chair of ASME's BPE Committee. "Back then, we were all using equipment originally made in Wisconsin to process milk, cheese, and other dairy products."

The dairy systems were designed with living organisms in mind. Their smooth surfaces, welds, and fittings were made for hot-water sanitization and self-draining cleanup.

"The industry was young and we didn't really know what we needed," Cirillo explained. "We knew we didn't want cracks or crevices where microbes could collect and grow. We needed surfaces that were cleanable."

The dairy industry's standard was the No. 4 finish polished with 150-grit silicon carbide or aluminum oxide sandpaper. "The problem was that, if the guy doing the sanding had arms like tree trunks and really laid into it, you'd get a very different surface from one done by someone with a lighter touch," Cirillo said. "How much pressure did they use? How old was the polishing wheel? What hardness did they use? The finishers varied all over the place."

End users and engineers had a difficult time even explaining their needs. "Engineers would talk to vessel manufacturers and we just couldn't relay our ideas correctly," Cirillo continued. "They were making vessels for the dairy industry, and when we wanted something else, we just couldn't describe it. There was an actual language barrier between what the owners wanted and what the manufacturer provided."

In 1988, Cirillo and a number of other bioprocessing engineers met at one of the industry's trade shows to discuss the problem. One year later, on June 26, 1989, they had formed the Bioprocessing Equipment Committee, to bring consistency in language, specification, design, fabrication, installation, and inspection.