Single-Use Technology

Standardization, Costs, and Other Industry Concerns

by Jerold Martin

Single-use technology began on the downstream side of bioprocessing, primarily in presterilized filter capsules and plastic biocontainers for buffers and media. Since then, it has expanded to upstream operations, including disposable bioreactors and mixers. The newest trend is to move further downstream into sterile formulation and filling. With the increasing popularity of disposable systems, some users are wondering what is being done to standardize the various components from different manufacturers and what BPSA (the Bio-Process Systems Alliance) is doing to address these and other industry concerns. Jerold Martin, senior vice-president of global scientific affairs at Pall Life Sciences and Chairman of the Board and Technology Committee for BPSA, discussed these topics with *BioProcess International*.

Standardization

BPI: Standardization is a major concern with single-use technologies; what are the main schools of thought about this?

JM: Standardization is an interesting concept. Some people are asking about standardization and interchangeability of components, which I believe comes from the standardization of stainless steel pipes, stainless sanitary flange fittings, and "Code 7" style filter housings. There were no proprietary positions on those designs — different companies made them, but there were no standards for dimensions and tolerance. Eventually ASME-BPE established standards for pipes and sanitary flange specifications. There is still no industry standard on Code 7 filter housings, however.

Single-use manufacturing involves many proprietary technologies for filters and sterile connectors, as well as formulations of biocontainer films and tubing. Although there is a standard for rating sterilizing filters, differences in filter membranes require product-specific validation of bacteria retention as well as compatibility and extractables. Filters are not interchangeable without that. Pall Life Sciences was first to introduce a sterile connector (the Pall Kleenpak connector), which was effectively the industry "standard" until other suppliers introduced alternative sterile connector designs. None of the suppliers can be expected to give up their proprietary positions, so if users really want to standardize on single designs or materials, they can decide which one they want to use and stick with that. It is prudent for security reasons to qualify an alternative supplier, including alternative filters, connectors, films, and systems designs.

Although generic design "standards" would make that exercise simpler, it is unlikely we will see standardized generic components in the single-use industry because of the proprietary nature of the technologies. BPSA is establishing consensus recommendations for best practices of validation and use so overall savings can be achieved elsewhere.

Some users are looking for standardization of system designs. Both users and suppliers can agree that minimizing the variety of systems in a facility can reduce purchasing, inventory, validation, and training costs while controlling the risk of error. For suppliers, system standardization makes manufacturing easier and lowers cost. However, the ease with which single-use systems can be customized makes design standardization a difficult concept for users to agree on, despite the advantages mentioned.

What we find instead is that even within a single company, each engineer wants systems customized on his or her designs, and we often end up supplying multiple variants to the same company. For example, we have one customer for tubing manifolds used in sterile formulation and filling for which we supply more than 16 different configurations to one location. Standardizing system designs or modular subassemblies can be easier to implement and less costly for users.

Economics

BPI: What work is being done to address questions of costs?

JM: Quantifying the economic benefits of single use has also been challenging despite the obvious advantages. BPSA recently published *Roadmap to Implementation of Single-Use Systems* (published in the April 2010 supplement of *BioProcess International* and available on the BPSA and BPI websites). When you try to quantify the monetary cost and savings for a single-use process or facility, it can be a difficult exercise because many factors involved in the cost of a stainless steel process or factory have yet to be captured. One example is the cost of making water for injection (WFI). The savings in WFI is quite significant with disposables, but although it's relatively easy to quantify water use, many companies find it difficult to determine the actual cost to make WFI. Economics can be driven more by capital and overhead use than operating cost. It is quite clear, however, that there are savings to be had, and decisions for single use are being made even when cost savings analyses are unresolved.

Extractables and Other Concerns

BPI: What other industry concerns remain top priorities?

JM: Extractables and leachables from single-use systems continue to be a major concern. BSPA published the first consensus guide in 2008 (available for free download at www.bpsalliance.org)

Continued on page 58

Continued from page 64
and conducted a training seminar for FDA's CBER and CDER shortly thereafter. Since then, many users have successfully followed the BPSA-recommended risk-based approach.

This spring, BPSA released an expanded guide to determination of extractables (also available online). The guide suggests consensus conditions for conducting extractions, describes methods of identifying and quantifying extractables as potential leachables, and makes recommendations for comparing supplier-provided extractables data for similar components from alternate suppliers.

Other activities for BPSA include developing consensus specifications for plastic sanitary fittings. These are seeing wider use, especially at larger scales. There are no industry standards on the dimensions of plastic sanitary fittings comparable with what we have for stainless steel fittings. Tolerances for plastic sanitary fittings must take into account mold shrinkage factors, and establishing consensus specifications will help control mold costs. BPSA is not a standards-writing organization, but it provides stimulus to standards organizations such as ASME-BPE and ISO.

We are also developing a resource page on BPSA's website where we'll post links to key articles, white papers, and standards being developed. We envision this to be a key location for people seeking balanced information on single-use manufacturing.

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