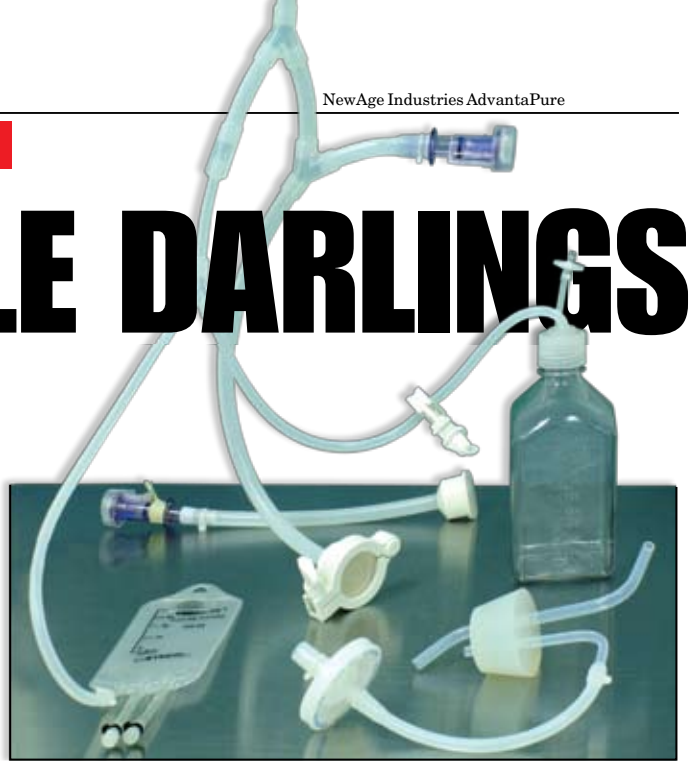
# DISPOSABLE DARLINGS

**Single-use equipment and systems are a growing trend among high purity processors. Here, the experts weigh in on the pros and cons of these up-and-coming disposable components**



NewAge Industries AdvantaPure

**FIGURE 1.** A single-use system like this one from can help reduce cleaning validation requirements, production downtime, and assembly time and costs

Not long ago, single-use bioprocessing equipment, such as disposable bags and tubing, appeared on the scene as an alternative to stainless-steel components for high-purity processing applications. Due to a fistful of benefits — including reduced costs, lower cross-contamination risk and increased flexibility — the use of disposables began to grow into a real trend among high-purity processors, especially those in the biopharmaceutical industry. With about 20% of the industry currently incorporating single-use components into at least one part of their processes, more and more processors are looking into the benefits, as well as the disposal drawbacks, and trying to decide whether single-use components and systems are right for them.

## A growing trend

Laboratory and clinical use in the biotech and biopharmaceutical industries currently accounts for the largest use of disposable technology, according to Bryan Downer, solutions expert with sanitary-system-design firm CSI (Springfield, Mo.). "Use in these biotech applications makes a lot of sense because there are a lot of change outs, and disposables allow this to be done quickly and efficiently," notes Downer. Also, he explains, there's not a lot of cost involved in infrastructure changes, and a lot of equipment is available for that scale.

However, according to a recent survey published by *BioProcess International* and available in detail on the Bio-Process Systems Alliance (BPSA) website (www.bpsalliance.org), adoption of single-use technologies has been significantly increasing in many processes beyond this arena.

The survey asked respondents in what processes they have adopted single-use technology and compared the data between 2008 and 2009. A marked increase can be noted in many segments. For example, use of disposables in upstream processing and media preparation jumped from 56.6% in 2008 to 62.9% in 2009. Use in cell culture and fermentation grew by leaps and bounds from 55.1 to 73.3% and in cell harvest and clarification from 43.4 to 56.2%, as well as in buffer preparation and hold from 52 to 63.8%.

Not surprisingly, implementation of all types of disposable technology has also seen growth, with even mature technologies enjoying significant increases in use. According to the survey, which asked respondents which single-use products or technologies have been implemented and again compared figures for 2008 to 2009, bioreactors have seen the most growth, up from 31.8 to 55.9% in just one year. Bags and bioprocess containers have also seen a significant increase from 76.3 to 87.3%, followed closely by mixers, which grew from 24.2 to 34.3%, and the connectors-, pipes- and tubing category, which rose from 56.1 to 64.7%. And, sensors, a relative newcomer to single-use technology, saw about a 7% increase in the year from 16.2 to 23.5%.

When asked why they implemented single-use technology, survey respondents cited cost savings, convenience, elimination of cleaning and sterilization cycles, reduction of contamination risk and flexibility. And with over 70% of the respondents reporting savings due to these benefits, it's easy to see why the use of disposables is growing so quickly.

## Big benefits

As the biopharm industry moves away from blockbuster drugs and into the realm of "niche busters," the inherent flexibility offered by single-use technologies will likely enable success and encourage growth of the industry, says Mani Krishnan, director of Mobius Single-Use Processing Systems with Millipore (Billerica, Mass.). "The new drugs aren't going to be like the large blockbusters of the past in the sense that the molecules are going to be more specific to a smaller population," he says. He explains that this trend is occurring because, as diagnostics improve, drug developers are finding that current drugs are only effective in a fraction of patients. So the newer drugs will cater to a smaller patient population, but there are likely to be more variants of the drug that will work for the rest of the patients. "A


Millipore

**FIGURE 2.** The Mobius FlexReady System family from Millipore includes equipment for buffer-media preparation, virus filtration and clarification. The company created entire systems to meet the needs of high-purity processors who are looking to move beyond single-use bags and tubing and into the realm of disposable process units

smaller group of patients means we're talking about going from developing drugs in a 10,000-L bioreactor to a 500 or 1,000-L unit. In addition to smaller batches, there will be changes in the way drugs will be processed," he says. "In the future, biopharm facilities will have to be more nimble so they can move from one drug product to another very fast. This type of batch processing is where we will see the adoption of single use going up significantly."

Bill Hartzell, business development manager with resin producer, Arkema (Philadelphia, Pa.), agrees. "There are huge benefits for single-use technologies as biopharm moves toward batch processing. Single use eliminates the need to clean the stainless-steel equipment between batches because you are getting systems that are all pre-sterilized," he says. "Also, you can have multiple products being made in the same facility, using the same infrastructure. And there are benefits during drug development, as well. As processors go through the phases of drug development and scale up to larger sizes, they do not have to build new infrastructure because single-use technology allows them to do multiple products under the same roof."

Another significant attraction to disposables is a reduced risk of cross contamination, says Jeff Chase, sales and marketing manager with SaniSure (Moorpark, Calif.). He says in a stainless-steel-based facility, contamination can be a factor, occasionally leading to loss of product. "We are told by customers in stainless-steel facilities that they lose between 5 and 9% of their product over the course of a year, but when they go to single use, that 5–9% is reduced to 1–2%," says Chase. "And when you're talking about a million dollar drug, a few percent drop in lost product is very significant."

The reason for reduced contamination risk is simple, says Ken Baker, CEO of NewAge Industries AdvantaPure (Southampton, Pa.). If you are making one product in a stainless-steel vessel that is not dedicated and switch to another product, it can lead to cross contamination of the first product into the second. Further, it is also possible not to rinse the cleaning agents properly. "Theoretically, the cleaning protocol in a stainless facility should be validated for proper rinse, but maybe one batch out of 1,000 could be cross contaminated and if that batch was worth $1 million, well, then you've just lost a million bucks," he says.

Reduced costs stemming from faster cleaning cycles and batch turnarounds are another advantage of disposable technologies. "The industry is starting to realize that single use has great benefits when it comes to reducing cleaning cycles," says Maik Jornitz, group vice president of marketing and product management for filtration and fermentation technologies with Sartorius-Stedim (Bohemia, N.Y.). "Many of the drugs are so highly potent that it requires a large volume of highly acidic cleaners to remove the residual drug components from stainless-steel surfaces and then you have to get rid of those cleaning agents," he explains. "On average it requires 8–12 h to clean and sterilize a typical 100-L tank. But if you use a 100-L disposable bag, you just rip the package open and have it set up and ready to go in 10, 20 or 30 minutes because it's pre-sterilized."

Baker reminds, "While you're spending all that time cleaning stainless steel, you're not making another batch. Turnaround is much quicker with disposables than with stainless steel, so processors can make more batches over the same period of time."

### The environmental aspect

There's much deliberation in the industry with regard to the environmental impact of disposable technologies and industry associations are working hard to determine the best path to take when disposing of the products. However, most maintain that despite the amount of plastic that needs to be discarded, disposable technologies are still more environmentally sound than traditional ones.

"What you see with single-use technology is a lot more visible waste," notes Krishnan. "However, traditional stainless-steel-based facilities generate a lot of waste that you don't see because it goes down the drain."

He and other industry experts say that when comparing the carbon footprint of stainless steel and single-use processes, single-use facilities are

## DISPOSAL OF SINGLE-USE SYSTEMS

The Disposals Subcommittee of the Bio-Process Systems Alliance recently published the Guide to Disposal of Single Use Bioprocess Systems to address the hot topic of disposal. The paper highlights the advantages and disadvantage of various disposal options, including the following:

- Landfill (treated and untreated): Landfill options offer the lowest operating costs, but are often perceived as environmentally unfriendly
- Grind, autoclave and landfilled: This practice is generally accepted as safe and helps reduce landfill volume. However, there is a significant capital cost and it requires additional handling
- Recycling: While this is environmentally appealing, it is impractical for mixed materials. Most disposables are made of mixed materials
- Incineration: This practice is also generally accepted as safe, but it may be legally restricted and can be costly
- Cogeneration: The most environmentally benign option, it offers some return on investment, but it may be legally restricted and presents the highest capital cost.
- Pyrolysis: This practice produces usable pure diesel fuel, which burns cleaner than that produced in a petroleum refinery. However, this is a very new technology, so few options are available. And its efficiency is rated as "subpar"

The paper, which discusses each option in detail is available for viewing on the organization's website. ❑

**SINGLE USE TECHNOLOGY AND SERVICE PROVIDERS:**

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|---|---|
| Arkema, Inc. | www.arkema-inc.com |
| BioProcess International | www.biprocessintl.com |
| BPSA | www.bpsalliance.org |
| CSI | www.csidesigns.com |
| Millipore | www.millipore.com |
| NewAge Industries AdvantaPure | www.newageindustries.com |
| SaniSure, Inc. | www.sanisure.net |
| Sartorius-Stedim | www.sartorius-stedium.com |

SaniSure

**FIGURE 3.** Single-use pre-fabricated bioreactor assembly kits help make setup of single-use bioreactors even faster, which will further the growth of that segment of the market

either equivalent or carbon positive when compared with traditional facilities. Facilities that use disposables are thought to be greener due to water and energy reductions that result from skipping the typical stainless-steel-related cleaning cycle.

As a matter of fact, SaniSure's Chase says that single-use facilities will typically see an 85 to 90% water use reduction over stainless-steel facilities. And because the water is not being heated for clean-in-place and sterilization procedures, says Chase, about 30% less energy is used to run a disposable-based plant.

Impressive sounding as this may be, most industry experts suggest that each facility do its own analysis to determine if it will, in fact, find these same favorable statistics. "We encourage customers to do their own analysis because the situation can be very different in terms of what a facility pays for electricity and water use," notes Krishanan. And on top of that, there's the aspect of dealing with the "visible" waste generated by the use of disposables. How this waste is handled ranges from facility to facility and from region to region. According to the BioProcess International survey the most common form of disposal is incineration, followed by landfill, waste-to-energy and, finally, conversion for alternative purposes. And many users combine disposal methods.

"Really, the focus should not be on what to do with the waste, but instead ought to be in understanding that there is waste in both types of processes," says Krishnan. "The question becomes how do you minimize waste? And there are easy ways to minimize the amount of plastic if you are smart about how you design your single-use systems. Most single-use systems in use today are not designed with the same amount of thought that goes into the design of stainless-steel systems. Optimal and intelligent design can significantly optimize the utilization of single-use technologies, and should be the focus, rather than what to do with all the waste that's sitting in the garbage can." ■

*Joy LePree*