

Union of Filter and Bag Makers Aligns with Bioprocessing Business Trends

by George Miller

Although hardly a topic of discussion among biotech executives and financiers during big-picture strategy sessions, filters and bags are nonetheless a staple of the biopharmaceutical industry. Any laboratory manager knows that the value of a steady and reliable supply of such commodities far exceeds its cost.

In its simplest terms, that's the idea behind the creation of Sartorius Stedim Biotech S.A., achieved at the end of June 2007 through the acquisition of bag-maker Stedim by filter maker Sartorius Group. But Sartorius Stedim Biotech CEO Joachim Kreuzburg prefers the term "combination" to "acquisition," however, in part to describe the unusual structure of the deal, but perhaps also for reasons of tact and cultural sensitivity.

"It's a cross-border reverse merger between a German and a French company," he said. "For most people, 'reverse merger' means nothing. We bring things together that fit very well. There's no overlap, and it's a very high level of strategic fit. Filters and bags are used in the same environment" (see the "Preparing for a Partnership" box).

Market dynamics also gave the deal a push. "For Stedim, the benefits of the acquisition became clear as customers were looking for solutions portfolios," said Kreuzburg. "For them it would be difficult to create such solutions by themselves. I think they have also seen that only a certain number of competitors will remain at the end. It was very much a strategic thought for them."

"The Stedim owners saw the consolidation and thought, 'the time is right to seize the opportunity to come together,'" added Reinhard Vogt, vice chief executive officer of Sartorius Stedim Biotech.

Stedim, a pioneer for disposable bag systems for biopharmaceutical applications, also has a product segment consisting of door systems for aseptic transfer technology and proprietary freeze-thaw technology.

Stedim chairman Bernard Lemaître said in an announcement, "once combined, Sartorius Biotechnology and Stedim Biosystems have the realistic ambition of forming the worldwide market leader for single-use technologies over the next five years."



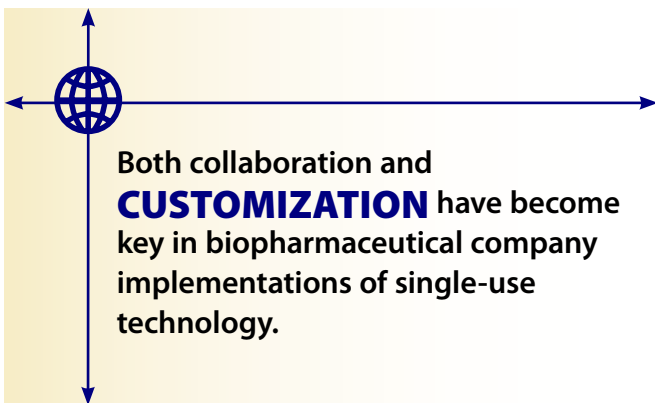
(WWW.SARTORIUS.COM)

The combination brings together under one corporate roof the manufacture of filters and bags — two complementary components always in use in bioprocessing facilities — not just to sell the commodities, but to integrate them as customers desire. Sartorius was already performing such integration services ad hoc for some of its customers, said Kreuzburg, but he sees the request for such services as a trend now among biotech manufacturers, and one in which he currently holds a competitive advantage.

In the acquisition deal, Sartorius carved out its filter-making and other bioprocess-related functions and "contributed" them to Stedim's bag-making operations, said Kreuzburg, simultaneously creating a central corporate function that oversees both the new Sartorius Stedim Biotech and the Sartorius Mechatronics Division, known for its laboratory balances and industrial scales.

The combination of the Sartorius Biotechnology Division and Stedim creates a global biopharmaceutical supplier with pro forma sales revenue of approximately €400 million anticipated for the year 2007. The company employs some 2,200 people.

Kreuzburg said that integration planning began well in advance of the deal's close, with management from both sides meeting to work out details. "We intensively used the four months between announcement and completion of this combination in order to prepare," he said. A lot had to be



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done to find the right transaction structure, according to Kreuzburg. “We, as the acquiring company, wanted to have significant financial firepower left.” He did not want to have to focus on reducing debt for the next several years.

“We think we are in a rather early, very crucial phase of our industry, and therefore we wanted to be prepared — and now we are prepared — for further strategic steps after the combination.” Such steps are likely to include acquisitions, partnerships and research and development efforts that build on the company’s reusable bioprocessing solutions, including fermentors, sensors and connectors in addition to filters and bags. The message to customers, he said, is that they get the two product portfolios, as well as the existing expertise and the potential for ongoing research and development work started at the separate companies.

Integrating elements of the two product portfolios dates back to 2001, said Vogt. “It came from a natural request from customers: ‘I want you two companies to work together. You are our preferred supplier for the filters and they are the preferred supplier for the bags.’”

The companies had a friendly relationship, said Kreuzburg, but not a very strong one. “The people in the market have met each other and have a high respect for one another. The products are complementary. It just happened that the culture of the two companies was also similar: average age of employees and background. And both are internationally minded companies.”

Kreuzburg said that the timing of this deal coincides with the spread of single-use technology throughout bioprocessing operations worldwide. “The executive level [at biopharmaceutical companies] is becoming open to disposable technology,” he said. “A decade ago we were working with the early adopters. More conservative companies are open to it now, but they expect solutions to be available [rather than just components]. They don’t want the task of integrating technologies.”

In fact, both collaboration and customization have become key in biopharmaceutical company implementations of single-use technology (1). “Process validation is always a team project — but the involvement of product vendors in implementation efforts makes it even more collaborative in nature,” wrote Cheryl Scott in *BioProcess International’s* disposable technology supplement. “Many users are working with their suppliers to find customized solutions to the issues their qualification and validation testing raise” (2).

PREPARING FOR A PARTNERSHIP

Sartorius Timeline, Bioprocess-Related Business

1870: Florenz Sartorius founds a fine-precision machine company and begins production of short-beam analytical balances.

1922: Company begins commercial production of separation and filter technology products.

1960: Sartorius uses the first machine for automatic manufacture of synthetic membrane filters.

1969: Plate-and-frame crossflow ultrafiltration system debuts for large volumes.

1976: Autoclavable, integrity-testable filter cartridge with a pleated membrane filter is unveiled.

1983: Automatic unit for integrity testing of membrane filter systems is launched.

1989: Large-area filter cartridge debuts with progressively finer, targeted filtration.

1999: Company acquires Vivascience (products for cell culture technology, protein purification and ultrafiltration).

2000: B. Braun Biotech International, manufacturer of fermentors, bioreactors and cell cultivation systems, is acquired.

2001: “Plant 2001” opens, for production of filters in Goettingen, Germany.

2007: Company acquires Toha Plast GmbH and secures access to plastics technology for biopharmaceutical disposables. Acquires Stedim and becomes Sartorius Stedim Biotech S.A.

Stedim Timeline

1979: Stedim S.A. is established in France.

1990: Company founds Stedim Inc in Concord, CA (USA)

1990: Company is registered as a Medical Device Manufacturer with the FDA.

1994: Stedim stock is listed on the Paris Stock Exchange.

1996: Stedim opens offices in Japan.

2001: Stedim Sarl manufacturing facility opens in Tunisia.

2003: Stedim opens corporate office building in France and doubles the Concord (CA) facility.

2004: Integrated Biosystems Inc. becomes a Stedim company.

2004: Acquires IDC (Isolateur Dénominateur Commun).

2006: Unifies business activities under the marketing name Stedim Biosystems.

2007: Company becomes Sartorius Stedim Biotech S.A.



Joachim Kreuzburg

THE INDUSTRY PERSPECTIVE

A recent survey of *BioProcess International* readers validates Kreuzburg's thinking. Disposable (single-use) technology is being adopted in most processes, with cell culture/fermentation, buffer preparation, and upstream processing/media preparation topping the list (Figure 1) (3). Some 70% of respondents said their companies have integrated single-use technologies into existing processes (Figure 2). Bags and filters were identified most often as the products used, followed by connectors, piping, tubing, and bioreactors.

Drug makers are adopting disposable technology for convenience: 85% of poll respondents said that the major factor leading to their company's decision to implement single-use technology is elimination of cleaning/sterilization cycles, followed by reduction of contamination risk, and flexibility (Figure 3). Cost savings, notably, scored near the bottom of the list of factors.

But poll respondents also expressed some concerns about the technology and identified barriers to adoption. Lack of experience and existing investment in stainless steel are by far the biggest barriers (Figure 4). Long lead times for custom disposable products was identified as a big headache (see the "Biggest Frustrations" box).

BIGGEST FRUSTRATIONS (3)

Question: What are your biggest frustrations with suppliers of single-use systems? Answers:

- Confusing catalog online
- Turnaround time for a custom configuration
- Not enough off the shelf products
- Reliability of hardware
- Each have areas that they specialize in and there is not enough competition to reduce prices; there is also not enough competition to compel companies to manufacture really high-quality equipment
- Not keeping up with demand
- Long lead times for custom disposable products are our biggest headaches
- Obtaining documentation
- Control of particulate material in bag chambers
- Big companies move too slowly. Small companies need more capital to provide faster turnaround.



Corresponding editor, George Miller (back, right) spoke about the creation of Sartorius Stedim Biotech S.A. with Reinhard Vogt (front, left), vice chief executive officer of Sartorius Stedim Biotech; Joachim Kreuzburg (front, right), Sartorius Stedim Biotech and group CEO; and Dominic Grone (back, left), group corporate communications.

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Figure 1: What processes have you adopted single-use technologies into?

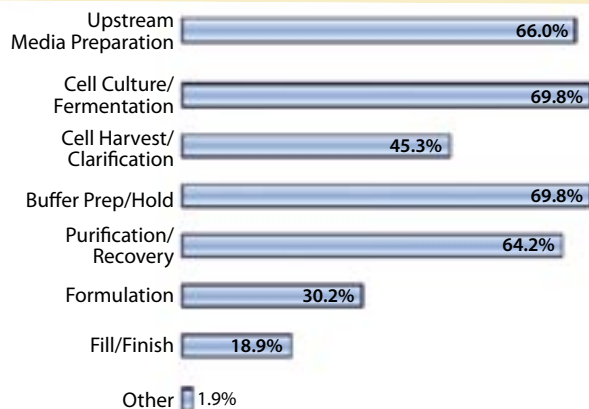


Figure 2: Has your company integrated single-use technologies into your existing processes?

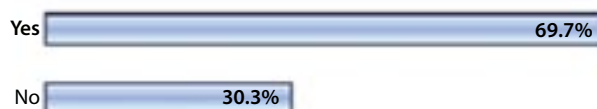


Figure 3: What were the deciding factors that lead to your decision to implement single-use technologies into your process?

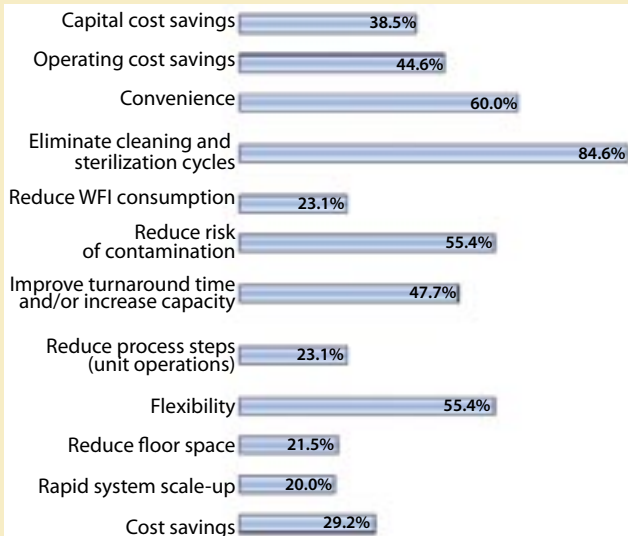


Figure 4: What are the biggest barriers to implementation?

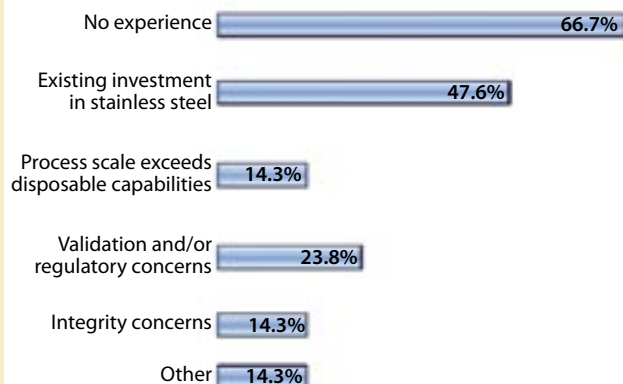
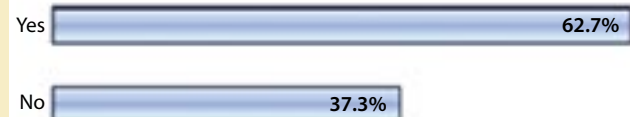


Figure 5: Did single-use technologies replace stainless steel systems?



Overall, the survey found that nearly 63% of respondents had used single-use technology to replace stainless steel systems (Figure 5). And although about 27% of respondents indicated they would spend \$100,000 or less on single-use technologies in the next two years, 35% indicated that they expect to spend \$500,000 or more (Figure 7).

From an industry perspective, BCC Research earlier this year pegged the 2006 US market for ultrafiltration membranes at \$635 million, up from \$579 million in 2005. At a compound annual growth rate of 7.4%, BCC expects the market to reach \$908 million by 2011 (4).

Those figures include both bioseparations/medical and municipal/industrial applications, according to BCC, with the market split down the middle. Bioseparation/medical applications have the higher growth rate throughout the forecast period. BCC said that in 2006 this sector was worth \$324 million and expected to grow to \$476 million by 2011, an 8% growth rate.

For the bigger picture, Kreuzburg uses IMS figures and company-generated market data, much of it based on information supplied by Sartorius Stedim salespeople based on conversations with customers. He anticipates 12% growth for his business this year, with the disposables portion growing faster than the rest. Some 10% of the company's filters today are assembled with bags, he said, which he expects to grow to 30% in the coming years.

From the Sartorius perspective, customer needs around disposable technology were a big driver for the acquisition.

"You can't develop everything by yourself," said Kreuzburg. "It takes too much time; it's too risky. For us as a company, it's very important that we have developed a cooperation strategy. Our R&D involves integration technologies."

A SMART FUTURE FOR DISPOSABLES

Kreuzburg said he believes that smart disposable devices are the future of bioprocessing. "Our customers more and more need to control processes in disposable devices," he said. "Today it's very difficult to measure certain parameters in disposables; it's a very young field in the applications. We think that these are the areas where we [Sartorius and Stedim] have combined power to offer the integrated solutions needed by the industry."

Sensors are key in improving process control, he said. R&D efforts currently include integration of oxygen and pH sensors in the form of small tags placed inside the bag, which of course eventually will be thrown away. Current work involves decoupling the measurement electronics from the sensor, so the latter can be thrown away.

"Our R&D engineers lack the not-invented-here syndrome, which is very typical for engineers, and I would

Figure 6: How much will your company spend in single-use technologies in the next 24 months?

CAGR of disposables ~18%
CAGR of the biotech industry ~12%
CAGR of the classical pharmaceutical industry 6–8%

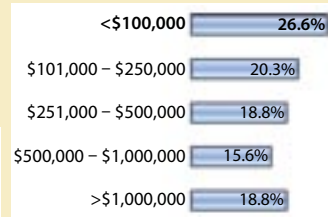
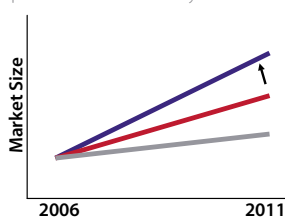
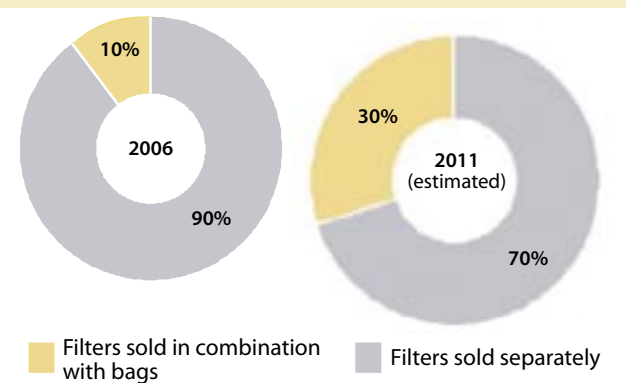


Figure 7: The market for disposables provides additional growth over the high underlying growth of the biotech industry (5). (SOURCE: SARTORIUS STEDIM BIOTECH)

Figure 8: Combination of filter and bag business supports growth prospects of combined company. Almost each bag is sold in combination with a filter, because a filter is always used when a bag gets filled with liquids. Of course, filters are also used in other applications. While both the filter and the bag markets are growing in absolute terms, it is expected that 30% of the filters will be sold in combination with bags by 2011 (5). (SOURCE: SARTORIUS STEDIM BIOTECH)



also say very typical for German engineers," said Kreuzburg. What they are doing is integrating technologies from the outside. And that is of course the key factor. It's not just that you get a piece of technology. It always has somehow to be integrated into our portfolio, and into a solution for our customers."

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George Miller is a corresponding editor for *BioProcess International*, geo.miller1@verizon.net.