

# Outsourcing OUTLOOK



## BIO Update

Jim Miller

The Biotechnology Industry Organization lends insight into the trends of biopharmaceutical contract manufacturing.

**T**he Biotechnology Industry Organization (BIO) held its annual meeting in Washington, DC, in June 2003 with approximately 16,000 people in attendance. The BIO exhibit hall is a good place to glean insights on trends in the biopharmaceutical industry. Here are a few tidbits that we picked up.

**Improving yields.** Improving the yields for bioreactor-based mammalian-cell culture is having a considerable effect on biopharmaceutical manufacturing. Expression rates of ~1 g/L are becoming the norm, nearly doubling the norm from two years ago, and individual instances of rates at 3–5 g/L are being talked about.

Improved yields are an important contributor to the easing of feared shortages in bioreactor-based cell-culture capacity (1). However, the increased yields are also dampening the prospects for a competing technology, namely, transgenic production. Proponents of transgenics have touted the technology as a more cost-effective alternative to bioreactor technology, especially for large-volume applications such as monoclonal antibodies. In particular, the capital costs of building up a transgenic herd of goats or cattle are a fraction of the investment required to build bioreactor trains to produce an equivalent volume of drug substance. However, the improving expression rates are halving and even quartering the amount of bioreactor capacity required to produce a given volume of material.

With the economic advantages of transgenic production quickly disappearing, proponents of the technology are emphasizing another supposed advantage—the ability to produce proteins and antibodies that are difficult to express in bioreactors. As long as this advantage holds up, it could preserve a niche for transgenic production, but the industry still must deal with regulatory uncertainties, concerns about animal safety, and worries about contamination of other crops for plant transgenics.

**Biomanufacturing and fill–finish capabilities.** Linking biomanufacturing and fill–finish capability seems to be a new trend in the manufacturing sector. During the BIO showcase sessions, **Baxter** (Deerfield, IL) announced that it is offering cell-culture manufacturing, using capacity at its existing manufacturing facility, to complement the fill–finish capabilities of its Baxter Pharmaceutical Solutions unit in

Bloomington, Indiana, and the delivery capabilities of its Baxter Global Drug Delivery business. **Cardinal Health** (Dublin, OH) revealed that the sterile manufacturing facility that it is completing in Raleigh, North Carolina, will contain clinical-scale cell-culture suites. **Boehringer-Ingelheim** (Ingelheim, Germany), **Abbott Laboratories** (Abbott Park, IL), and **DSM N.V.** (Heerlen, the Netherlands) have separate-but-complementary units that offer biomanufacturing and fill–finish capabilities. The linking of biomanufacturing and sterile fill–finish capabilities is clearly aimed at offering smaller biopharmaceutical companies a “one-stop” manufacturing solution.

**More small-molecule and API contract manufacturers.** One of the more telling signs of the direction of the biopharmaceutical industry was the number of small-molecule process development and API manufacturing contractors in attendance. The list included **Albany Molecular Research** (Albany, NY), **Peakdale** (High Peak, UK), **Siegfried** (San Diego, CA), and the custom manufacturing unit of **Cambrex** (East Rutherford, NJ). The presence of these firms is a clear sign that biopharmaceutical companies are diversifying their development portfolios to include small-molecule compounds.

Some small-molecule manufacturers indicated that the business downturn they have been experiencing over the past three years may have bottomed out. Although no one wanted to get overly optimistic just yet, executives indicated that requests for proposals and new project activity from both big and small pharma has been improving in recent months, with one business development executive saying that their early stage business has been up almost 10% in the past three months. Another company official indicated that his company was seeing more projects but at a smaller average project size than in the past.

### Financing activity heading upward

One reason for increased contractor activity may be the improving financial markets. Small and mid-sized pharmaceutical and biopharmaceutical companies picked up the pace of fund-raising in June 2003, achieving the highest volume of new investment in more than 12 months. According to the data collected for PharmSource’s Contractors Lead Sheet service,

companies raised \$2.9 billion in June 2003, more than double the \$1.3 billion raised in April 2003, which was the second highest month from the previous 12 months. As a group, biotech stocks were up 18% in the second quarter of 2003, buoyed by several new product approvals, which is what may be driving renewed investor interest in the sector.

The big boost in new funds came from private debt placements, which accounted for \$2.2 billion of the \$2.9 billion total activity (76%). Given the sharp decline in interest rates in recent months, the jump in debt financing is not surprising. **Cephalon** (West Chester, PA) made the biggest deal, which raised \$600 million for repayment of older outstanding debt. An additional 15 companies raised \$1.6 billion, which is an average of \$100 million each. Most of the money was raised in the form of convertible debt, meaning that the holders can convert the debt into equity (shares of common stock) at a future date.

There was also an upswing in equity deals in June 2003. The \$610 million raised in private and public equity offerings was the most equity raised in more than 12 months. Forty-one private placements were announced in June 2003 versus an average of 18 placements/month during the previous 11 months. In addition, \$175 million was raised in three public offerings.

The jump in new capital entering the industry should be a boon to CROs and contract manufacturers, because a shortage of funding has caused a rash of project cancellations and drug company liquidations during the past 12–24 months. It remains to be seen, however, whether the business environment has improved for the long-term or whether companies have been taking advantage of a brief window of opportunity. The use of convertible debt suggests that investors are still wary of many companies’ viability and are hedging their bets. A better indication of sustained investor confidence will come from the reopening of small pharma/biotech initial public offering activity, which has been dormant for almost a year.

### References

1. J. Miller, “Capacity Worries Fade for Biomanufacturing,” in *Outsourcing Outlook, Pharm. Technol.* 27 (7), 82–84 (2003). **PT**

Jim Miller is president of PharmSource Information Services, Inc., and publisher of *Bio/Pharmaceutical Outsourcing Report*, tel. 703.914.1203, fax 703.914.1205, info@pharmsource.com, www.pharmsource.com.