management. The first revamp traded in cows for continuous cell-culture systems employing hollow-fiber membranes; this second shift involves turning Bio-Response's technology into a money-making business.

Now under the direction of Vaughan Shalson, who was previously vice president of marketing for the Cutter Biologicals division of Miles Laboratories (Elkhart, IN), Bio-Response currently sees itself as a "service supplier" rather than just a contract producer of monoclonal antibodies and recombinant proteins. What's the difference? Shalson explained that the company's scientists were excellent at cell culture, but "did not have a great commercial sense." The firm had been performing services such as cell-line optimization and custom design of its client's production systems without charging for these *per se*. Now, Shalson describes the company as "a full-line supplier of mammalian cell-culture services." This means that as part of its "Parallel Process Development" program Bio-Response will act more like a business and bill and market its services accordingly. Shalson added that the company has increased its fees to be more in line with industry averages.

Bio-Response's new president and

chief executive officer also hopes that a cost-control program will provide some relief to the bottom line—staff will now have to water their own plants, for instance, rather than rely on a service, and employees will be washing more glassware as Shalson phases out many of the more expensive disposables.

Still, the real albatross around the firm's neck has been its cash-draining, proprietary tissue plasminogen activator (t-PA) project. Shalson reported, however, that the company is finally close to signing up a pharmaceutical partner for t-PA. And he sees Bio-Response emphasizing its service component over proprietary proteins for at least the next 1–2 years.

"Scientists are not real good at focusing on pragmatic applications," echoed Robert Ivy, president and CEO since July of Ribi ImmunoChem (Hamilton, MT). Ribi has long suffered from low recognition due to its out-of-the-way location and its unusual focus on detoxified bacterial endotoxins as adjuvants—created by so-called molecular engineering—especially in the treatment of cancer. Ribi's Detox™ is already in clinical trials against malignant melanoma and common and genital warts; colorectal, pancreatic, and lung cancer

trials should also begin this year. And the firm's Ovamid™ is in the clinic versus ovarian and colorectal cancers, with bladder cancer trials slated for early '88.

Ivy—who was previously president of Oncogene Sciences (Manhasset, NY)—views Ribi's immunostimulants as falling into two categories: "directed" (such as with cancer and vaccine adjuvants), and general (such as boosting patients' immune systems prior to infection-prone surgeries or radiation therapy). The healthcare veteran sees adjuvants for vaccines against infectious diseases as the quicker, surer way to market. He believes that it is difficult for scientists to recruit the body's own immune system to fight cancer because this disease is a relatively recent problem—that is, people used to die of other causes before cancer had a chance to strike. Infectious diseases, however, have been around long enough that the body is better adapted to deal with them. He notes that Ribi's adjuvants could be used as a pre-treatment for hospital patients to prevent or ameliorate septic shock. And at the end of last year the firm signed an agreement with the U.S. Army to supply Ribi's adjuvants for a potential malaria vaccine. —Arthur Klausner

JAPAN ROUNDUP

Scientists at the Biological Engineering Laboratory of Teijin Ltd. (Osaka) have mass-produced chimeric antibodies that contain murine light- and heavy-chain antigen binding domains linked to human light- and heavy-chain constant regions. Since these chimerics consist largely of human sequences, they should interact with the immune system in a fairly normal way and not elicit the harmful immune response caused by some mouse monoclonals used in therapy. Completely human monoclonal antibodies would be ideal to prevent immune responses in patients but are difficult to produce directly. Teijin makes its chimerics via hybridomas grown on a large scale in a novel, two-cylinder culture system that allows continuous production and simplified purification.

Synthetic sulfonated polymers have proved effective in inhibiting the growth of AIDS virus and cancer cells, as shown by collaborative work done by the research groups of To-shiyuki Uryu at the Production Tech-

niques Research Laboratory of Tokyo University, Naoki Yamamoto at Yamaguchi Medical School, and scientists at Ajinomoto's Central Research Institute. Although many polysaccharide derivatives are known to inhibit the growth of cancer cells and viruses, most have very low potency and cause unwanted side effects. In contrast, the sulfonated polymers—synthesized by a "dry sugar" sulfonation process carried out under high vacuum—inhibit transcription with high potency and seem to be relatively free of side effects.

The three classes of polymers with the highest anti-viral and anti-cancer cell potency are branched polymers of xylose (xylofuranan: average molecular weight 7,000), ribose (ribofuranan: average molecular weight 10,000), and glucose (dextran: average molecular weight 34,000). The researchers showed that sulfonated polymers of xylose and ribose effectively inhibit reverse transcriptase and RNA polymerase. Sulfonated polymers also inhibit the growth of the AIDS virus by 70–90 percent

when present at a concentration of 10 milligrams per milliliter, and 90–98 percent at a concentration of 100 mg/ml.

Ajinomoto (Tokyo), one of the world's leaders in lymphokine research, has demonstrated in mouse experiments that B-cell stimulating factor-2 (BSF-2) significantly increases the effectiveness of vaccines. Injecting this lymphokine along with vaccines doubled the amount of antibody initially produced and increased by 11-fold the amount of antibody produced following a second exposure to the antigen. The Ajinomoto scientists, working in collaboration with Tadimitsu Kishimoto's research group at the Protein Engineering Center of Osaka University, found that BSF-2 strengthens the immune response primarily by enhancing the proliferation of B lymphocytes.

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