As first reported in last month’s column, aaiPharma’s (Wilmington, N.C.) board of directors launched an investigation into apparent irregularities in the sales reports of two of its proprietary products, Brethine and Darvocet. Although the board had not finished its investigation at press time, published reports indicate the problem may have been “channel stuffing” (i.e., shipping far larger quantities of a product to wholesalers than what is actually sold through retailers and institutions). The problem is similar to the one Bristol-Myers Squibb faced two years ago.

The announcement triggered a series of negative events, including the resignation of CEO Philip Tabbiner, a delay in the filing of aaiPharma’s annual 10-K report with the Securities and Exchange Commission, and a possible government investigation. The company dodged a bullet when it secured a new $40-million credit line after its principal secured lender blocked its existing $100-million revolving credit facility. It subsequently arranged a new $135-million, two-year revolving credit facility.

The developments cast a cloud over what seemed to be a successful effort by aaiPharma to transform itself from a CRO into a specialty pharmaceutical company focused on pain management products. For 2003, aaiPharma reported $283 million in revenues, of which sales of proprietary products and contract services accounted for $180 million (64%) and $86.5 million (31%), respectively. These reported revenues—and aaiPharma’s true financial condition—are now in doubt. A major concern is how the company will manage the $339 million debt that it accumulated to buy its proprietary product line.

Although aaiPharma’s crisis stems from problems in its proprietary products business, the services business will be deeply affected by the fallout. The two lines of business operate under a single corporate umbrella and share R&D facilities and staff. Consequently, the services business will be subject to any financial obligations or constraints that arise from resolving the current problems. Financial obligations and constraints could include financial restructurings, cost reductions, and shareholder lawsuits.

It seems likely that in the aftermath of the current crisis, aaiPharma will reemphasize its services business, which has been explicitly deemphasized in recent years during its transition into a specialty pharmaceutical company. An informal survey of AAI Development Services competitors did not reveal a rush by current AAI clients to find alternative outsourcing arrangements. Undoubtedly, senior management has moved quickly to allay key clients’ fears of a near-term bankruptcy filing by securing its new line of credit. However, current and prospective clients will be analyzing its financial statements and prospects with renewed care.

The aaiPharma situation highlights issues that pharmaceutical companies should consider when assessing a potential outsourcing partner. When the services business is just one part of the contractor’s total operations, clients should have some familiarity with the financial status of the other business operations as well. The company’s corporate structure—such as whether businesses operate under a single corporate entity or as separately incorporated subsidiaries—could be important.

An obvious concern is the stability of the contractor’s financial condition. aaiPharma finished 2003 with a lot of debt and little cash. Being so highly leveraged, the company had little room for management error or an unfavorable change in market conditions. Changing strategy on top of a highly leveraged financial structure simply compounds the business risk.

Preclinical update

Preclinical CROs were upbeat following this year’s annual meeting of the Society of Toxicology (SOT), held in Baltimore, Maryland, in March. CRO executives say the market is much stronger than it was last year, which started off poorly but ended on a high note. According to Andy Slack, director of sales and marketing for CTBR, Inc. (Montreal, Canada), demand is...
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especially strong for specialty toxicology studies such as drugs delivered by means of injection, infusion, and inhalation. The demand can be attributed to the large number of protein-based drug candidates and the solubility problems of many small molecule drugs in the pipeline.

The major announcement during SOT was a three-year agreement for toxicology services between Covance Inc. (Princeton, NJ) and an unnamed major pharmaceutical company. Under the agreement, Covance will build out and dedicate an entire floor of its Madison, Wisconsin, laboratory to its client’s studies. The work will be performed by Covance staff, but the client will have several of its staff on site at all times, including, most likely, a study director and quality assurance personnel. The client will determine what kinds of studies it will perform in the facility.

Under the agreement, Covance will receive a minimum of $45 million in fees from the client for work completed in the dedicated facility. The total revenues could be much higher, depending on the number of studies that are performed and the additional services purchased from Covance (e.g., bioanalytical testing). According to industry sources, the challenge for Covance and the client will be to carefully manage the facility’s usage so that both parties receive the full value from the reserved capacity. According to Wendel Barr, Covance’s group president of Early Development, North America, the agreement required nearly a year of discussions between Covance and the client, despite their existing and successful long-term relationship. Barr says that the deal represents a unique confluence of factors, including the client’s long-term need, the contractor’s uncommitted space, and the standing relationship. Given the strong demand for limited preclinical capacity in the industry, the deal will be difficult to duplicate in the near term.

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The technology can be used with medications treating both the anterior and posterior chambers of the eye. For example, to treat retinal disorders, the electrostatic attraction serves to pull the drug from the cornea and conjunctiva, which acts as a reservoir, and to migrate it through the sclera to the retina.

According to Martinez, many topically delivered ophthalmologic medications are deliberately formulated with low concentrations of the active ingredient because higher concentrations will cause the eye to tear. This tearing can then wash out some or all of the active drug molecules. However, Novagali Pharma’s emulsions also have high-moistening properties that help lessen eye irritation.

The formulation contains a new excipient, “oleylamine,” which is responsible for the positive charge. “We had to partner with big players to combine a new compound with a new excipient that would work chemically,” says Martinez. Creating two phases—one oily and one aqueous—is the first step in the manufacturing process. When each mixture reaches 60 °C, the two are mixed together to form an emergence. This emergence consists of large droplets (~1–5 μm in size). Then, a high-shear stirring process decreases the size of the droplets to ~1 μm. A high-pressure homogenization step then forms 150-nm droplets. Finally, the formula is filled into bottles, and autoclaved.

Several of Novagali Pharma’s products are now in Phase II clinical trials, including treatments for dry eye, age-related macular degeneration, and other retina-related diseases. Plans to formulate other potent lipophilic drugs such as antiinflammatory, glaucoma, allergy, antibiotic, and antiviral products, are in the works. According to Gregory Lambert, PhD, Novagali Pharma vice-president of research and development, one over-the-counter product for the treatment of moderate dry eyes should be on the market by 2006.

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