

plementary information, this time within six months of the registration. On the basis of that information, the Medicines Division would decide whether the product could remain on the market. (Those data have now been submitted.) A number of other national authorities—including Italy's—have adopted a similar approach, and the new data will, according to Guiseppe Vicari, be discussed by the CPMP before the end of this year. The future of Proleukin in Europe depends now on the assessment of data gathered post-CPMP approval.

The Dutch have found a different mechanism for reassessing Proleukin. In its original decision, The Netherlands had given what was the closest to being a wholehearted approval for IL-2; in principle, every doctor could prescribe the drug. But Hans Schellekens of TNO (Rijswijk, The Netherlands) says that the National Health Council's General Committee on Immunomodulators, of which he is a member, has just published an interim report which outlines some of the difficulties with IL-2—the side-effects, the need for intensive care, the need for an immunology laboratory. "This is advice to the Minister of Health, who will probably follow it. It will limit treatment to, at most, eight academic centres in The Netherlands. It would not surprise me if it was only three." Schellekens believes that government officials were frightened by what they had done in approving Proleukin and that they will now take this opportunity to curb its use.

In trying to understand why the normally cautious Dutch authorities were originally enthusiastic about IL-2, other critics point to the possibility of economic influences over the IL-2 approval decision. The government—in part through its for-profit MIP Equity Fund, which is backed by Dutch financial institutions—helped arrange \$5–10 million in low-cost loans and subsidies to entice EuroCetus to locate in Amsterdam. The impression given was of "a lot of economic muscle flexing...by the national government when the scientific and medical facts were not so clear," said one observer. "If you look at the data and the number of patients treated, it's surprising that the authorities were so lenient on IL-2."

The next decision of the CPMP on Proleukin, to be taken in the next few months, could go either way. Vicari believes, however, that "the further decision of the CPMP and the final decision of the FDA may come to the same point...The decision in one re-

gion should influence that in the other since both are based on scientific principles."

That return to science would be widely welcomed. One interpretation of the current regulatory disparity with IL-2 is that Europe found itself

confronted all at once with a new drug, a new company, and a new regulatory system. In seeking success for all of them, judgments on the acceptable risk/benefit ratio of the drug itself may have been skewed by other factors. —John Hodgson

INSTRUMENT MARKETS

APPLIED BATTLES EARNINGS DROP

NEW YORK—Blue skies have turned cloudy for automated instrumentation leader Applied Biosystems (Foster City, CA). Recent profits have fallen short of the Human Genome Project windfall predicted by analysts: Earnings-per-share estimates of \$1.30 for fiscal '90 actually panned out at \$0.43, with flat sales. This triggered a dramatic correction in the stock price, which dropped to 8 from last year's high of 35. And last month Applied closed its Ramsey, NJ bioseparations branch. The company will take a charge of \$5 million against first-quarter earnings for severance and relocation costs as a result of the move.

Three factors seem to underlie the downturn. In September 1989, prior to an expected fourth-quarter downturn in profits, the company warned investors that robust 1988 sales figures were due mainly to a big payout from Japan, related to pressures to redress the trade imbalance. This situation ended as the dollar strengthened. Also, competition in Japan from Hitachi (Tokyo) may have diluted Applied's market share, company officials said.

Second, the analytical instrument business as a whole saw the results of tight money, as budget cuts affected both universities and private companies. "Anyone selling an over-\$100,000 instrument will suffer," says First Boston analyst Amy Berler.

Third, a sort of hiatus has set in following heavy bouts of instrument purchases in the past several years. "These products are no longer revolutionary, as they were five years ago...people may be waiting for next-generation machines before they venture to buy again," she adds.

Loss in market share in the protein synthesis area, which carries the biggest price tags, contributed much to the lack of growth in sales this year, according to company officials.

Despite falling profits, Applied's R&D spending remains high. President Andre Marion told analysts that rather than cut costs, he will try to boost revenues by 15 percent this year. Nonetheless, in merging its Ramsey, NJ liquid chromatography

unit with an existing San Jose (CA) facility, Applied is relocating only 20 percent of 113 workers. The move, according to vice president G. Bradley Cole, was made "both for cost savings and to help focus new product development in one location."

How long will the downturn last? Long enough for biotech and medical technology analysts to put a "hold" on Applied shares. Berler says she does not advise customers to hold on to stocks that long. "The timing involved could mean unhappy clients. But if [the stock price] goes down more, it becomes more of an attractive bargain. While the market is saturated, customers will buy something with either better accuracy; the same accuracy but more flexibility; or less reagent use," says Berler. "ABI has exposed just the tip of the iceberg. There will be a market for an improved instrument."

Applied continues to introduce such new instruments, including most recently an integrated amino acid analyzer and new versions of its popular PCR-Mate DNA synthesizer. And with little debt, it can afford to make strategic acquisitions, such as its purchase of Bio-Ion, maker of a vastly improved type of mass spectrometry (see "Materials and Methods," this issue). Another ace in the hole is the licensing of the TRW fast data finder chip.

Takeover speculation based on the deflated stock price was given some substance with Marion's statement to analysts that he'd consider selling the company as a last resort. Other manufacturers of DNA and protein sequencers and synthesizers would be likely buyers. In assessing possible suitors, Berler sees no obvious choice. "Perkin-Elmer looks good on paper, but there is some culture clash between the two companies; Hewlett-Packard has a cultural and geographic fit, but are slow on acquiring; Millipore seems to have a 'not invented here' attitude; and Pharmacia, which likes to acquire and recently launched its own DNA sequencers, could benefit from Applied's many service locations." —Pamela Knight