THE LAST WORD/

JAPANESE PHARMACEUTICAL
BIOTECHNOLOGY: PERCEPTION VS. REALITY

by Henry I. Miller

What's this?" you may well ask. "Is *Bio/Technology* devoting more editorial pages to examining what the U.S. can do to stave off the Japanese takeover of biotech? We've heard it all before." Throughout the 1980s rumors and speculations on whether Japan will come to dominate in biotechnology world-wide have run the gamut. Depending on who you talk to, the U.S. is safely out front; the Japanese are breathing down our necks; or they have (essentially) already won the race. But—in all this time—few of these speculations have been based on fact. And the fact is this: the Japanese are worthy opponents, but they are not a threat.

The U.S. Food and Drug Administration (FDA) recently conducted its own survey of Japanese pharmaceutical R&D (see *Bio/Technology* 7:326, Apr. '89). The data clearly show that—despite a high level of activity in Japanese industry—the U.S. does, indeed, have the lead in developing biotechnologically derived pharmaceuticals.

FDA surveyed Japanese companies developing pharmaceuticals via recombinant DNA (rDNA) technology, hybridomas, cell culture, and the chemical synthesis of biologically active proteins. Sixty-four such companies responded affirmatively to the survey. They ranged from established, vertically integrated firms to those testing products for their foreign affiliates. The roster also includes traditional food or petrochemical companies attempting to diversify into pharmaceuticals. It is obvious that the Japanese pharmaceutical industry—and the government—have devoted massive resources to adapting biotech production methods: nine therapeutics or vaccines already have marketing approval, and approximately 134 other products are in various stages of research, development, or clinical testing. And the road to product approval in Japan is no less tortuous than it is in the U.S.: developing a new drug takes years and costs tens of millions of dollars.

Japanese companies have concentrated their efforts on certain groups of products. These include agents that prevent or break up blood clots (16 products); anti-viral vaccines (10); immuno-stimulatory interleukins (8) and colony stimulating factors (7); and interferons for treating viral infections or cancer (7). In fact, cancer is a major focus—well over half the products in R&D appear to be for treating cancer *per se* or related conditions.

Overall, the survey results make several important points. First, although the Japanese are applying the tools of biotechnology to new drug development with zeal, the U.S. still holds a significant lead—two-to-three times the number of companies and the number of products. According to the Pharmaceutical Manufacturers Association's (PMA, Washington, DC) October 1988 survey, 54 U.S. companies have produced 106 products, either already approved for marketing or in clinical trials. In Japan, our survey identified 24 companies with a total of 45 products at comparable stages. While PMA's survey does not include any products that have not yet entered the clinic, FDA's does: overall, the 64 Japanese respon-

dent companies have 143 products—many of which are still in early development or pre-clinical animal trials.

Second, there remains no hint of products that could require new regulatory paradigms. And with a large number of products yet to enter the regulatory pipeline, both the U.S. and Japan are committed to building the infrastructure capable of evaluating these products.

Finally, the fact that, in both countries, new biotech drugs have progressed successfully from the clinic to the corner pharmacy attests to healthy economies and public regulatory policies—reasonable enough to permit product testing and approval.

Given that the Japanese effort is so robust—along with their legendary success in other industrial sectors—why does that nation lag behind the U.S. in new drug development? What explains the differences in R&D? One factor that certainly lends American companies an edge is the highly competitive entrepreneurial atmosphere in which they operate. The 400-odd "biotech" companies in this country outnumber all those in the rest of the world—combined. That provides a tremendous source of creativity, and the drive to "get it done" faster and smarter than one's competitors.

Second, the regulatory environment in the U.S. most likely contributes to its lead. From the beginning, FDA has treated biotech-derived products no differently from similar products manufactured by other means. The Agency has articulated this policy clearly and often. FDA sees no need for new procedures or requirements to regulate biotech products. In fact, under standard regulations biotech products have so far been approved in about half the time it takes for their "traditional" counterparts. And FDA continues to streamline its review process, instituting changes advantageous to the manufacturers of biotech products.

By contrast, the Japanese government still treats biotechnology as "special," and *not* equivalent to traditional technology. Here the emphasis is on process rather than product. Japanese agencies used to require case-by-case approvals of any fermentation larger than 10 liters that uses rDNA-containing organisms. Even today, the Japanese Ministry of Health and Welfare regulates the production of pharmaceuticals made from recombinant organisms more stringently than similar products from other sources. While this illogical, process-based approach is probably more an annoyance than a deterrent to Japanese industry, we must wonder to what extent it has dampened corporate ardor toward biotechnology. In our experience, a rational and science-based approach can serve not only as an end in itself but also as a way to avoid regulatory disincentives.

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