policy analyst John Pike of the Federation of American Scientists.

The panel's attempt to understand Observer's silence was hindered because telemetry from the spacecraft was turned off before the pressurization of its fuel tanks as it prepared to enter orbit around Mars. That was done to safeguard a few vital components, a protective move the panel concluded could have been avoided with a better design. Nevertheless, after sifting through 60 potential failure scenarios, the panel settled on four that were associated with the pressurization procedures. The most probable hypothesis is that two tablespoons of a fuel component, nitrogen tetroxide, leaked through "check" valves during the 11-month voyage. Then, during pressurization, the chemical reacted with another fuel component, monomethyl hydrazine (MMH), to rupture tubing within the propulsion system. This rupture, spraying out MMH and liquid helium, would act like an uncontrolled thruster, placing the spacecraft into a spin and disrupting communications.

As for management failures, the panel called Observer's design "generally sound," but it faulted NASA for using too much hardware and software and too many procedures designed for near-Earth satellite missions on a much more ambitious and rigorous interplanetary voyage. "The fundamental problem was they thought the spacecraft itself was low-risk," says Pike, suggesting that more attention was placed on Observer's instruments than on its platform.

A second major criticism centered on the use of a firm fixed-price contract between the Jet Propulsion Laboratory (JPL), which managed the mission, and Martin Marietta Astro Space (formerly RCA Astroelectrics and General Electric Astro-Space Division), which built the craft. Originally, Observer was part of a planned series of Mars visits in which a different payload of instruments would be launched on almost identical platforms. But Congress balked at the overall price tag and the mission became a one-shot deal that demanded constant redesigning as instruments were added and Observer grew in complexity.

In that situation, a fixed-price contract was "inappropriate," says Coffey, since it placed pressure on the contractor to limit redesigns and consultation with JPL because that would drive up costs. The panel made a strong recommendation for future NASA missions: "Do not use fixed-price contracts when development is required, or when changes are anticipated, or when control over technical implementation is required." As NASA plans new planetary missions, including another try at Mars in 1996, those words—and many others in the report—will garner close attention.

–John Travis

U.S.-JAPAN COLLABORATION

Academic Biotech Deals Offer More Promise Than Product

BOSTON—In 1989, when Japanese cosmetics maker Shiseido Co. agreed to spend a record $85 million over 10 years for a new center on skin research at Massachusetts General Hospital (MGH), some biotechnology analysts saw it as the leading edge of a new wave of Japanese investments in basic biomedical research at U.S. universities. The fear that U.S. universities were providing Japanese companies with an entree into biotechnology intensified the next year, when Hitachi Ltd. funded a $20 million research center in the same building as the biochemistry department at the University of California (UC), Irvine.

TOM CARROLL

Windows of opportunity. Hitachi's bold investment has yet to be matched by other Japanese companies.

But the wave appears to have broken with barely a splash. The Cutaneous Biology Research Center (CBRC) in Boston and the Hitachi Chemical Research Center Inc. in Irvine are bold attempts by the Japanese to open a window on basic biomedical research—an area where Japan lags far behind the United States. But 4 years later, they remain the only Japanese investments of that magnitude in biomedical research at U.S. universities, and the only ones of any significant size not targeted at developing a particular product or drug. Neither has achieved the degree of success that might keep policy analysts up nights worrying about the independence of U.S. academic research or the health of the U.S. biotechnology industry. "What are Hitachi and Shiseido getting back?" says Mark D. Dibner, director of the Institute for Biotechnology Information in North Carolina. "Why would anyone want to do a similar deal now? The return in biotechnology has not been that astounding."

In fact, the lack of return is only one of several reasons why Japanese companies haven't followed in the footsteps of Shiseido and Hitachi. (A 1992 report from the National Research Council cited 28 biotech investments in the past decade by Japanese companies in U.S. universities, most for less than $1 million.) Within Japan, companies wanting to invest in biotechnology—whether already in the health care business or relative newcomers to the field—face formidable obstacles. The recent global recession, which has lingered in Japan, has left chief executives with little appetite for risky ventures of any type, much less in another country. Japanese companies also recall a string of failed attempts during the 1980s to develop products from research collaborations with U.S. start-up companies. What's more, any successful transfer of technology must overcome steep cultural hurdles, including the disparate research styles of U.S. and Japanese laboratories. "It takes a long time to set up a special system to acquire the technology. I'm not so optimistic," says Masato Mitsuhashi, a diagnostics researcher at the Hitachi center.

Heading home. Hitachi officials know firsthand about those obstacles. A project Hitachi funded at Irvine indicated that the receptor antagonist N-methyl D-aspartic acid may be a promising treatment for those with brain damage. But the company, which must obtain written approval from UC Irvine before pursuing any developments growing out of its financial support, did not exercise its first rights to license the technology. The reason: It couldn't afford to spend the amount—as much as $100 million—needed to conduct clinical trials. Instead, it invested about $150,000 in a venture company charged with the task. In addition, Hitachi has no infrastructure for marketing biotechnology to match what it has developed over decades in electronics and chemicals, further reducing its chances of success.

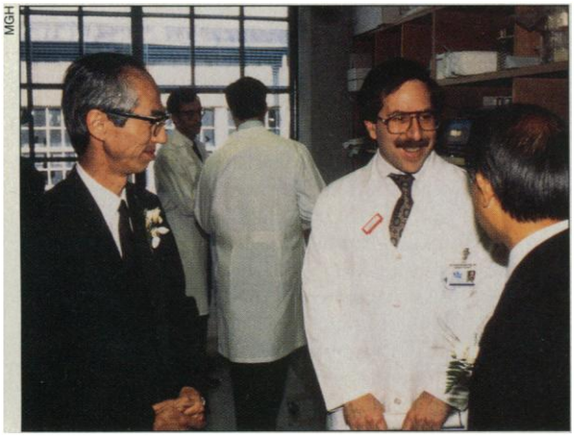
Hitachi's reticence to exploit its Irvine connection is reflected in the resources the company is putting into the venture. The Hitachi lab in California, which has room for 80 researchers, employs only 15, all Americans. Four Japanese scientists working there

were sent home recently after Hitachi cut the lab's $7 million annual operating budget by almost 30%.

The story is similar at Shiseido's center in Boston, which was established to learn more about how the skin works. Although the company has not reduced its $9 million annual funding of the lab, any return on its investment remains a distant hope. Because the center's work is considered fundamental research, none of the 80 researchers in the lab has been pressured to develop any products. Shiseido has first rights to discoveries made at the center, but after 4 years it has yet to receive a patent on anything coming out of the center. (Seven applications are pending.) And the company has not met its quota of placing five scientists at the center, although officials hope to reach that level early this year.

The difficulty of working in an unfamiliar field with uncertain payoffs is exacerbated by the rules of corporate Japan, which put service to the company ahead of individual scientific accomplishments. Because Japan lacks a postdoctoral educational system, many scientists are trained on the job as company employees. But these "salarymen" have no job descriptions and are moved around frequently, especially during tough economic times. "If you are hired as a scientist, you may end up as a salesperson," says Mitsuhashi. That strategy poses quite an obstacle to research projects requiring years to complete.

Even scientists who return to Japan after working abroad find it tough going. Pressure to conform and work within a group outweighs rewards for individual, innovative achievement—the very attributes that created and now sustain the U.S. biotech industry. And despite adopting a corporate mentality, researchers rarely share ideas or engage in the type of animated discussions that foster new ideas. "In Japan, you can't tell your professor or boss that his idea is wrong because you will lose your job," says Toshihiko Hibino, a CBRC biochemist who is visiting from Japan. "You also have to work harder in the United States. In Japan your position in the company is protected, so job competition is not as severe and you don't need to write papers and work so hard."



Welcome. MGH's Richard Grandstein thanks Shiseido's president, Yosiharu Fukuhara *(right)*.

Spanking new. A typical laboratory at the Cutaneous Biology Research Center in Boston, funded by Shiseido.

Indeed, many Japanese scientists who did excellent work in the United States become invisible upon their return to Japan, says CBRC-Shiseido liaison Yasuhisa Nakayama, a skin biologist who returned to Japan after studying at Harvard University. "I disappeared," Nakayama says about his attempt to stay in touch with those on the cutting-edge in his field. My supervisor said I didn't need to talk to [scientists at] Harvard."

As the company's liaison with the skin center, Nakayama doesn't want to repeat that mistake. So he encourages CBRC scientists to pursue the most advanced work and keep in touch with research projects from around the world when they return to Japan. "If Shiseido really wants to be a global corporation, including in R&D, we need scientists working with outside countries. The actual communication is as or even more important than the research we get from CBRC," he says.

Once burned, twice shy. Some industry analysts think the difficulties facing Japanese companies in making U.S. university research pay off are part of a larger problem of underestimating the inherent risks of supporting scientific exploration in biotechnology. Several companies made large investments in the early 1980s in U.S. startup companies in an effort to leap-frog the lengthy and costly research stage of product development, but few paid off. "There are no hard numbers, but I think the Japanese have spent a huge amount of money [in U.S. biotech startup companies and joint ventures] and haven't gotten their money's worth," says Alan G. Watson, an analyst at Oxford Partners in Stamford, Connecticut, who tracks foreign investments in U.S. biotech ventures.

Some companies appear to have learned a lesson from those unsuccessful ventures: set up their own research operations on U.S. soil and use their physical proximity to build stronger ties to the academic community. That's what the pharmaceutical firm Tanabe Seiyaku Co. did after spending more than $20 million in 1988 to help Immunetech Pharmaceuticals of San Diego develop an anti-allergy peptide that never passed Phase III clinical trials. It purchased the company's research arm, renamed it Tanabe Research Laboratories USA, and put the lab to work on inflammation treatments using cell adhesion and cell activation inhibitors.

But a poor track record hasn't deterred all Japanese investors. Among the leaders is Kirin Brewing Co. Ltd., which has seen its small investment in Amgen, of Thousand Oaks, California—helping to develop EPO to treat anemia and granulocyte colony-stimulating factor (G-CSF) to fight infections—pay off in $300 million worth of sales of the two drugs this year alone in Japan. Kirin has set up more than 20 research collaborations in the United States in the past decade, including the nonprofit La Jolla (California) Institute for Allergy and Immunology. Although the payoff to date has been small, the company seems ready for the long haul.

"Most of these efforts have failed," says Koichiro Aramaki, vice president of Kirin's pharmaceuticals division in Tokyo. "The possibility of research success is small, even for in-house research. If you take 20 research collaborations and one or two are successful, this is enviable."

That strategy may be fine for a large company such as Kirin, which divides its money among several small research sites. But few Japanese companies in today's economy are willing to emulate Shiseido and Hitachi and take the plunge with a multimillion-dollar investment in a U.S. university. North Carolina's Dibner isn't surprised. "I think there's a lot of value in the Shiseido-MGH arrangement," he says. "But that value is potential, so [the results] are still a crap shoot."

–Lori Valigra

Lori Valigra writes about science and technology from Cambridge, Massachusetts.