INDIA

# New Rules Push Researchers Closer to Biotech Industry

NEW DELHI—Biotechnology in India seems to have everything going for it. Universities and research institutions have developed an impressive product list, ranging from pregnancy and blood-type tests to diagnostic kits for hepatitis B, typhoid, and parasite infections. And there's a burgeoning indigenous market for biotechnology-based health care, expected to reach $1 billion by the end of the decade. But over the past 5 years, product after product has failed in the marketplace. Now the Indian government has set out to change that record, with a set of new policies designed to increase the chances that its investment in biotechnology—$200 million over the past 10 years—will yield commercially viable products.

The new guidelines were endorsed last month by a scientific advisory committee to the Department of Biotechnology (DBT). They require that almost every application submitted to the government meet three criteria: The work should be world-class; it should involve collaboration with industry; and it should concentrate on areas that can be patented. In addition to their emphasis on research that is likely to prove commercially valuable, the new policies also create a mechanism for independent peer review of DBT-supported projects, a step now taken only rarely. "If the goal during the past 10 years was to build infrastructure, the new priority will be demand-driven research," says Chitaranjan Bhatia, DBT's secretary.

With a current budget of $30 million, DBT contributes about 60% of the government's support for biotechnology research at universities and national labs. The rest comes from the Council of Scientific and Industrial Research, through support of specific projects and infrastructure. Medical products and processes account for two thirds of the total spent on biotechnology.

Although the money spent may have added to India's storehouse of knowledge, it rarely led to marketable products. Biotechnology officials say that failure is rooted in decades-old policies that reflected the deep distrust between academic scientists and industry, combined with an almost allergic reaction by researchers to applying for patents. (That reaction was triggered in part by Indian laws that, until this year, have prohibited the awarding of product patents.) "India has great potential in medical biotechnology," says microbiologist Anand Chakrabarty of the University of Illinois, Chicago, a member of DBT's overseas advisory committee. "But it lacks the culture of industrial research and development."

In particular, funding agencies and scientists seldom consulted with industry before launching research projects. "Government labs first developed products and then offered them to industry," says Padmanaban Balaram, a molecular biophysicist and peptide chemist at the Indian Institute of Science in Bangalore. The result has been a string of unsuccessful technological products that were rejected outright by Indian companies or were inferior to those from the United States and Europe.

**All business.** Delhi's Vijay Chaudhary hopes to sell rights to his monoclonal antibodies.

For their part, many scientists blame companies for an overdependence on foreign technology. "The biotechnology industry has preferred the less risky and more profitable option of relying on proven technology from abroad," says Bhatia.

But those attitudes on both sides are changing, say officials, as companies prepare for proposed new laws that would bring India in line with international practices that permit product patents (*Science*, 10 March, p. 1419). The concept—familiar to Western scientists but new to India—is for companies to build ties with leading researchers who, while working in areas of commercial interest, remain free to pursue intellectually challenging research. "A few biotech companies are contacting labs and even proposing joint research," says Balaram.

The trend, which predates the new guidelines, can be seen in labs throughout the country. "Even 2 years ago, we would have been hard-pressed to identify a single case of joint research," says Prasanta Ghosh, director of DBT's division of products and industrial development. Today, he says, at least a dozen groups from academic centers around India are collaborating with industry.

Balaram is on the leading edge of that movement. He has a grant from a major pharmaceutical company, Dr. Reddy's Research Foundation, to study biological properties of fungal peptides. "The idea is to look for molecules that might lead to novel synthetic peptide drugs," he says. "It is essentially open-ended research supported by industry." In a similar vein, scientists at the Institute of Microbial Technology in Chandigarh have received support from a Bombay-based biotechnology company to optimize a process for making recombinant clot-dissolving streptokinase, and a New Delhi pharmaceutical company has proposed a joint research effort with the Indian Institute of Chemical Biology in Calcutta on the immunomodulatory efforts of certain plant compounds. At the National Institute of Immunology, which is funded by DBT, director Sandip Basu is trying to develop a macrophage-targeted drug delivery system to use against infections.

Drug companies are also recognizing the importance of research in both expanding local market share and gaining a toehold in the international scene. Several large companies have set up biotechnology divisions for in-house research on new drugs and immunodiagnostics, and the country's largest, Ranbaxy Laboratories, has refocused some of its 200 scientists on novel drug delivery systems and stem cell–based therapies. It's also raised its overall spending on

**COMMERCIAL PROMISE: JOINT PATENT FILINGS IN THE PAST YEAR***

| Team Leader/Institution | Topic |
|---|---|
| Vijay Chaudhary<br>Delhi University | Monoclonal antibodies for phase display and protein engineering |
| Asis Datta<br>J. Nehru U., New Delhi | Use of *Amaranthus* gene for superior blend of proteins in transgenic crops |
| V. P. Malhotra<br>Shriram Institute for Industrial Research, New Delhi | Surface active plastics for diagnostic plates and tissue culture (2) |
| P. V. Sundaram<br>Voluntary Health Services, Madras | Process for stabilization of enzymes used in biotechnology |
| Anil Tyagi<br>Delhi University | Vector for controlling expression of proteins in mycobacterial systems |
| Debi Sarkar<br>Delhi University<br>(filing pending) | Technique to deliver genes into liver cells using animal virus as vector |

* Patents filed by research institution and Department of Biotechnology
SOURCE: P. GHOSH, DEPARTMENT OF BIOTECHNOLOGY, 1995

R&D since 1991 from 3% to 5% of sales.

DBT's emphasis on patenting as well as publishing is already beginning to pay off. Since January, DBT officials have helped five researchers with patent applications in biotechnology, and University of Delhi biochemist Debi Sarkar is preparing one on a technique that uses a genetically altered animal virus as a vector to deliver genes into liver cells (see table). "Six patents in 6 months from a single agency is a record in India," says Ghosh, whose agency is paying the cost—$5000 or more—of processing each patent. DBT is also negotiating with a U.S.-based biotechnology company for the rights to a set of monoclonal antibodies developed by Delhi's Vijay Chaudhary and used in a process that expresses foreign proteins on the surface of a virus.

The optimism about India's future in biotechnology is tempered by funding restraints. DBT's budget has grown by only $2 million in the past 2 years, and Bhatia admits that the department has not succeeded in pruning its lengthy list of research areas in medical biotechnology. "The prevailing situation of too few resources, spread too thin, will continue," he predicts.

In the face of tight budgets, the government wants to be sure that scarce funds are used to meet pressing national needs. "A lot of the work in the coming years will be aimed at developing products that are either not available from abroad or not suitable for India," says Prakash Tandon, head of a government task force on medical biotechnology. That means that continued support for the age-old problems of bacterial and parasite infections will divert some funding from research in such "new" areas as phage display technology, cytokine research, cancer at the molecular level, and human genetics.

Old or new, the research will be subject to a peer-review system meant to improve the quality of work at government-sponsored labs. The new system will enlist outside bodies, chosen either by DBT or the Indian Council of Medical Research, to review work on a regular basis. Already this spring, an HIV diagnostic kit developed at the DBT-funded International Center for Genetic Engineering and Biotechnology in New Delhi was tested by microbiologists at the National Institute of Virology, Pune, and at two hospitals before it was transferred to industry.

The more rigorous peer review is meant to reinforce the government's emphasis on scientific excellence. "We're telling scientists and industry that the only route to global competitiveness is innovation," says DBT's Ghosh.

**–Ganapati Mudur**

Ganapati Mudur is a science writer in New Delhi.

VIETNAM

# Joint Dioxin Research Imperiled

The freshly opened diplomatic ties between the United States and Vietnam are supposed to usher in an era of normal relations between the two former enemies. But don't try telling that to an international team of biologists, sponsored by the National Institutes of Health, who visited Vietnam last month to study the health effects of a defoliant used by U.S. forces during the Vietnam War. On 30 June, customs officials at Hanoi airport seized most of the research material collected during the trip, which explored potential collaborations to trace the impact on the population of Agent Orange, an herbicide contaminated with dioxin.

Among the confiscated items were blood and tissue samples that were to be tested for dioxin. This sort of analysis "is critical to any work done in Vietnam," says team leader Christopher Portier, a computational biologist at the National Institute of Environmental Health Sciences, which last year was ordered by Congress to explore potential research ties with Vietnam. However, only a few labs worldwide—and none in Vietnam—are capable of sophisticated analyses of dioxin, says University of Toronto pharmacologist Allan Okey, another member of the team.

The visiting researchers were given no reason for the seizure, although there are rumors that the incident reflects a feeling among some government officials that pursuing the matter—regardless of its potential scientific value—could jeopardize future ties with the United States. Until the U.S. State Department "figures out what went on," says Portier, he will delay any recommendation on whether the agency should participate in research projects with Vietnam.

The airport incident was only one of a series of problems encountered by the team, which was co-sponsored by the World Health Organization and was comprised of nine scientists from Canada, New Zealand, and the United States. Vietnamese officials twice delayed the trip, and 1 day before Portier left he was told by an official of the National Institute of Occupational and Environmental Health in Hanoi—the team's host—that "presentations on dioxin would not be allowed" at a 3-day pesticides conference in Hanoi. "We were wondering what the nine of us were supposed to talk about," says Arnold Schecter, a professor of preventive medicine at the State University of New York's Health Science Center and a member of the team. "The Vietnamese scientists [at the conference] were pleasant, but it was as if they were killing time."

Despite these hurdles, the Western scientists met individually with Vietnamese researchers and found "fantastic" opportunities for collaborations, says Paolo Toniolo, a professor of environmental medicine at New York University. Potential topics include exploring a link between birth defects and maternal dioxin levels and examining associations between Agent Orange exposure and cancer incidence as tallied by Vietnam's fledgling cancer registry.

ARNOLD SCHECTER

**Unaccustomed trouble.** Arnold Schecter hopes airport incident won't affect work with Hanoi's Hoang Dinh Cau.

But the immediate fruits of the trip never cleared customs. The officials seized a range of materials, including 40 blood samples from people exposed to Agent Orange in Laos, 26 samples of Vietnamese food—such as milk, fish, and beef—destined for a lab in Amsterdam, Netherlands, to be analyzed for dioxin, and scientific papers and other documents prepared by Vietnamese scientists. The customs officials "were clearly looking for anything that smelled like dioxin," says Toniolo. Schecter, who has made a dozen trips to Vietnam, said this was the first time Vietnamese officials have confiscated biological specimens from him.

As *Science* went to press, the State Department was still trying to broker a deal to have the materials released. "I'm hoping this turns out to be a tempest in a teapot," says Dennis Harter of State's Vietnam desk. But Harter says "it's up to the Vietnamese scientists and the authorities to work out" arrangements for future shipments of biological specimens.

Much good science will be lost if such arrangements cannot be made, say Western scientists. "Vietnamese dioxin scientists have been trying for years to get a group like ours to discuss dioxins," says Schecter. "But it's impossible to plan experiments of good quality if you have this kind of uncertainty."

**–Richard Stone**