GENE THERAPY

Varmus Proposes to Scrap the RAC

Harold Varmus, director of the National Institutes of Health (NIH), has decided that the government's method of reviewing gene therapy needs to be drastically simplified. In a policy to be announced this week, Varmus is suggesting that it is time to "dissolve" the NIH's Recombinant DNA Advisory Committee (RAC) and end the practice of subjecting each proposed new clinical gene therapy trial to public review. RAC—which includes lawyers, ethicists, public representatives, and clinicians—has served for 8 years as the final gauntlet that gene therapists must clear before getting approval to start a clinical trial.

Instead, Varmus would like to leave detailed safety analyses to others—including the closed-door reviews of the Food and Drug Administration—while focusing NIH's attention on big issues. He hopes to appoint a small group of experts to meet several times a year to advise NIH on gene therapy. In addition, Varmus says, NIH should sponsor regular public workshops examining such questions as whether it's wise to treat fetuses with gene therapy or to use HIV as a therapeutic "vector." Varmus unveiled his plans on 9 May at a meeting of gene therapy researchers in Hilton Head, South Carolina; later he confirmed them in a phone interview with *Science*.

RAC's impending demise has drawn criticism from some prominent gene therapists and current RAC members. But Varmus says that while the panel "did serve some function" in the early days—assuring the public that risks of genetically engineered products were well understood—he believes that it has outlived its usefulness. The two most recent RAC meetings (scheduled for March and June) were canceled because no novel experiments were submitted for approval. In any case, Varmus said, RAC had begun to exhibit a taste for trivia: It often got bogged down in debates over the wording of patient consent forms. "I don't think we can any longer justify the need for an NIH-based approval process," he argues, adding, "I'm not sure it was ever appropriate."

Varmus notes that in proposing to do away with RAC, he is following the recommendations of two expert advisory groups he commissioned last year. Both of them suggested that NIH should treat gene therapy no differently from other types of biomedical research. Indeed, some panelists said the fuss over gene therapy had given the public an overblown idea of its efficacy (*Science*, 15 December 1995, p. 1751). In addition, NIH is tightening up its coordination of intramural research on gene therapy, as the panels recommended, and encouraging studies on basic vector biology.

The announcement that RAC may soon disappear did "not elicit any cries of protest" from the gene therapists at Hilton Head, says Nelson Wivel, the virologist who serves as RAC's executive director. He was in the audience during Varmus's speech and sensed that the clinicians were "not unhappy to hear that they would have fewer hoops to jump through." Wivel is casting his own vote against RAC, in a way. Six weeks ago, he announced that he will be leaving RAC's staff and quitting the government (he also serves as chief of NIH's office of recombinant DNA activities). On 1 July, Wivel will become deputy to one of the best known gene therapists in academic medicine, James Wilson of the University of Pennsylvania.

RICK KOZAK

Broad view. Varmus says NIH should look at issues, not protocol.

Varmus's announcement did spark some dissent, however. W. French Anderson, a former NIH gene therapist now at the University of Southern California, calls the proposed closing of RAC "shortsighted, inappropriate, and wrong." Anderson says RAC's public reviews have "provided the public with confidence that genetic research is being done in an open and appropriate way." While Anderson agrees with Varmus that RAC should not focus on "routine protocols," he thinks it should review and pass judgment on the use of "significant new technologies."

Hematologist Brian Smith of Yale University, a current RAC member, favors efforts to simplify the process. But, echoing Anderson, he argues that Varmus's proposed public workshops ought to focus on actual—not hypothetical—proposals. Smith says, "When you talk about science, you talk about a specific experiment." The RAC "has served its function well because it is so specific," Smith believes, suggesting that it should play the role of a Supreme Court, taking up only exceptional cases. Abbey Meyers—president of the National Organization for Rare Disorders, a RAC member, and a patients' rights advocate—worries that unethical practices will increase if gene therapists are not kept under close scrutiny.

Both skeptics and advocates will have a chance to pass judgment on Varmus's plan. According to staffers, NIH will publish a summary of it in the *Federal Register* this week and allow 15 days for discussion. Then, more likely than not, NIH will terminate RAC.

–Eliot Marshall

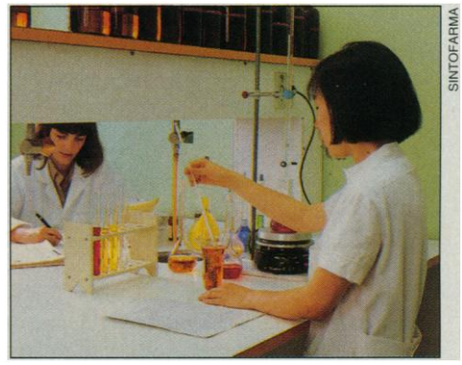
BRAZIL

Patent Law Closes Drug Loophole

SÃO PAULO—After a 5-year debate, Brazil has finally adopted a new patent law that extends intellectual property protection to foods and pharmaceuticals. The law, which was expected to be signed this week by President Fernando Henrique Cardoso, should put an end to the widespread practice in which Brazilian laboratories copy patented drugs and sell them freely in Brazil—the world's sixth largest market for pharmaceuticals. Supporters say the new law should stimulate outside investment as well as build up a homegrown drug industry. But critics contend that it is likely in the short run to have the opposite effect—to drive commercially useful research offshore or into the hands of multinational companies because of the absence of local capacity.

Passed by the legislature last month, the law aims to bring the country in line with international practices. It also relieves tension with the United States, which has been lobbying for stronger intellectual property rights. "Brazil has done the right thing," says a spokesperson for the Pharmaceutical Research Manufacturers of America. "We see it as a model for the rest of Latin America and the world."

While Cordoso says that the law is a step away from a "colonialistic mentality," many groups fought the measure on the grounds that the low level of R&D spending by Brazilian firms will give foreign-owned companies a chance to lock up all commercially valuable research. "We are not competitive," says Sara Kanter, technical director of the Association of the National Pharmaceutical Laboratories in São Paulo. "Our industry is still in the copy-and-innovate phase, and our market share does not allow us to have capital enough to invest in research." She predicts that the law will lead to "90% of the Brazilian academic research [in the field] being absorbed by multinational companies."



SINTOFARMA

Private property. New law ends a drug company's freedom to pirate patented products.

Kanter's group and many other organizations, including scientific societies, were especially angered by a clause that extends protection to existing patents that have not yet yielded marketed products. This so-called "pipeline" provision would prevent a Brazilian lab, for example, from someday copying a product patented by a U.S. or British drug company that is still under development. Companies have 1 year to submit their existing patents for revalidation by Brazilian authorities.

Senator Ney Suassuna, author of a previous version of the law, argues that the pipeline principle will damage Brazil's commerce and scientific research. But Francisco Teixeira, a lobbyist for an organization representing 31 multinational companies, says that the provision "can't damage something that does not really exist. ... It will protect not only foreign research but the little research done in Brazil as well."

Many groups were also troubled by a provision allowing the patenting of microorganisms. They protested that Brazil's enormous genetic assets—its vast biodiversity—would eventually be owned by multinationals. In the end, the language was modified to apply only to transgenic organisms—what Kanter calls a "little victory."

The new law is expected to wean Brazilian scientists from their current practice of going overseas to patent their discoveries. Sérgio Ferreira, a pharmacologist at the University of São Paulo and one of the country's most-cited researchers, holds a British patent on an analgesic that inhibits interleukin-1. He filed in Britain because the work was done in Britain and, in any case, it could not have been patented in Brazil. The substance is undergoing toxicological tests by a company that aims to market it. While Ferreira hopes that the new law "will create a patent mentality among researchers that will stimulate research," he is also president of the Brazilian Society for the Promotion of Science (SBPC), which fought against some aspects of the legislation. "It might not have a harmful effect on research," says Ferreira diplomatically. "The question now is how to carry out the new law with the proper commercial perspective."

–Cláudio Csillag

Cláudio Csillag is a science writer in São Paulo.

MOLECULAR BIOLOGY

Unique Protein Database Imperiled

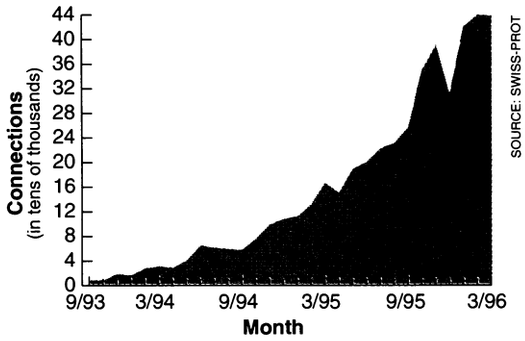
Molecular biologists around the globe got a surprise e-mail last week, urging them to send messages of support for one of their most important databases: SWISS-PROT, a database of amino-acid sequences of naturally occurring proteins, pioneered by Amos Bairoch of the University of Geneva. The database, and others associated with it, has been plunged into crisis by the failure to win a development grant from the European Union (EU). Bairoch and his colleagues are now seeking emergency funding to keep the publicly accessible database from being sold to a private company, and they are warning that if no funds are forthcoming, SWISS-PROT could be shut down by the end of June.

"As it stands, the situation is extremely bleak," says Graham Cameron, head of services at the European Bioinformatics Institute (EBI) near Cambridge, United Kingdom, a key partner in the development of SWISS-PROT. "To lose SWISS-PROT now would be like losing access to the Internet. It is a tool that so permeates life in molecular and cell biology that everyone depends on it," says James Garrels, president of the biotechnology company Proteome of Beverly, Massachusetts.

SWISS-PROT has proved increasingly valuable to researchers who want to analyze protein structures and look for similarities to other proteins. It now contains the sequences of more than 50,000 proteins, consisting of more than 18 million amino acids, and it carries a high level of information about the sequences, such as a description of their function, domain structure—common three-dimensional subregions of proteins—and other features useful for researchers. "It's a vital tool for a lot of our research," says Mike Waterfield, head of the Ludwig Institute of Cancer Research in London.

Waterfield's assessment is borne out by the number of queries SWISS-PROT receives. SWISS-PROT was the first molecular biology database to connect to the World Wide Web in 1993, and its main server attracted about 7000 users in September that year. So far this year, it has been logging more than 400,000 connections per month. SWISS-PROT also acts as a reference for other databases, and their future may also be uncertain if new funding cannot be found, says Bairoch.

The funding problem stems from a decision 2 years ago by the Swiss government, which had been supporting the database, to seek a European or international partner to share the costs. Switzerland said that it would continue to fund SWISS-PROT only if international funding were found. Bairoch and his team sought a grant of $1.9 million from the EU, to be matched by $1.4 million from Switzerland, for a 3-year development program. But EU officials told the database team last week that the proposal, while scientifically sound, did not have high enough priority to justify funding. "Without the EU funds the Swiss will not pay up," says Cameron. "I guess the EU may not have realized the significance of their decision," adds Bairoch. But a Brussels official says that the EU was not happy with this funding arrangement in Switzerland.



Heavy use. More than 40,000 researchers now connect to SWISS-PROT each month.

So Bairoch and his colleagues are turning to the user community while continuing to seek alternative sources of funding. "I'm talking to a couple of pharmaceutical companies that are interested, but my main wish is to see the database remain in the public domain," says Bairoch. The European Molecular Biology Laboratory in Heidelberg, Germany—the parent organization of EBI—is also wary of private ownership. "It's very much at odds with our mission," says Cameron. And some industrial scientists agree. Jonathan Knowles, European director of research at Glaxo Wellcome, Britain's biggest drug company, believes that the information should remain in the public realm: "The sequence data represent an enormous leap forward for biomedicine, and it's important everyone can have total accessibility to the data."

The team is now hoping that a resounding vote of support from users will help persuade Swiss and EU funders to continue supporting the database. So far, the response has lived up to their expectations: Within hours of publicizing their plight on 10 May, Bairoch had received hundreds of e-mails, including one from Harvard University Nobelist Walter Gilbert. But many researchers are hastily assessing the damage should the database be lost. "You could get by without SWISS-PROT if researchers wrote their own programs to search different databases," says Waterfield. "But it'd be like going back to the Dark Ages." Molecular biologists should know within the next 6 weeks whether the Dark Ages are a prospect or not.

–Nigel Williams