servants) whose workplaces are being reorganized would have had the right to sue the government. The judicial system would have crashed.

"Abwicklung," or winding up—popularly regarded as a way of removing the rights of people being made redundant—was agreed to by both East and West German governments before unification and, at first glance, appeared to have won the approval of the Supreme Court when it ruled on the practice in April. But it seems that the Berlin government did not read the fine print of that ruling as closely as did Humboldt University's endangered faculty.

University officials noticed that the court wrote: "The winding up of a facility implies its disintegration." In legal terms, that means that either the body disappears altogether or it is taken over by another body, neither of which has happened to the Humboldt University.

With that technicality behind them, 700 of 2522 tenured staff whose departments had officially been wound-up in December are now once more secure in their old jobs. This has infuriated longtime opponents of the old regime. At Berlin's Free University—founded in 1948 by professors and students forced out of the Humboldt by political pressure and now competing with the Humboldt for scarce research funds—there are calls for the "complete disintegration" of the Humboldt. That, of course, would be lawful.

It is not a suggestion that the Humboldt takes kindly. For Heinrich Fink, a theologian and freely elected president of the Humboldt, the issue is whether the Berlin government should have a say in the closure of university departments—whether they contain appointees of the old regime or not. He is sure to fight for the university's right to settle the matter in its own way.

The Berlin government is not simply going to leave the matter to the university. Aware that the Humboldt disagreement may prove a test case for other east German institutes where the policy of "fire-and-rehire" has been used, Berlin's senator for science and technology, Manfred Erhardt, is instead going to try to win the case in the courts. If necessary, he states, he is determined to take the case all the way up to the Federal Administrative Court, where issues of civil administration can be settled at the national level.

But this could prove a dangerous gamble—the case may take years to settle and if the government loses, Erhardt will have set a precedent with very costly repercussions.

■ RICHARD SIETMANN

Richard Sietmann is a free-lance science writer living in Berlin.

Promising AIDS Drug Looking for a Sponsor

Citing corporate strategy, Hoffmann-La Roche has decided not to pursue a compound that has excited AIDS researchers

AIDS RESEARCHERS ARE GENERALLY LEERY of expressing a lot of enthusiasm for new therapies, for fear of raising false hopes. But listen to their testimonials about a new compound that blocks the action of a viral protein called *tat*:

"From everything I know and have seen, and I have personally worked with the drug in vitro, it looks like a very promising and exciting compound," says virologist Douglas D. Richman of the University of California at San Diego.

"If it really is a relatively safe inhibitor of *tat* function or *tat* expression, it sounds like a fantastic way to approach the problem," says molecular biologist Robert C. Gallo of the National Cancer Institute.

"It's a very tantalizing approach," says Martin Hirsch of Harvard Medical School, chairman of the AIDS Program Advisory Committee to the National Institutes of Health.

So with this much enthusiasm for the drug, surely its developer, international pharmaceutical giant Hoffmann-La Roche, is pulling out all the stops to rush it into clinical development, right? Wrong. Apart from one small phase I toxicity trial at Johns Hopkins University Medical School in Baltimore, the new drug, code-named RO 24-7429, is going nowhere. The company has apparently decided that it would not make an adequate profit by developing and testing the drug itself and is trying to license it to another company. Roche spokesman Paul Oestreicher says several companies have expressed interest, but so far there have been no takers.

The story of RO 24-7429 illustrates the difficulty of setting public health policy when legitimate corporate interests are at odds with public health priorities. Roche scientists began looking at a *tat* inhibitor as a potential AIDS therapy in 1987. The federal government, through the AIDS program at the National Institutes of Allergy and Infectious Diseases (NIAID), agreed that the work was promising, and has been providing about $700,000 a year for basic research on the *tat* protein to a consortium of groups headed by Roche since September 1988. Two other companies are also working on anti-*tat* drugs, but they are said to be not nearly as far along as Roche.

The reason there is such interest in an anti-*tat* drug is that it represents a completely new approach for attacking the AIDS virus (see box). The tat protein binds to a specific site on the virus's own RNA and promotes the expression of other genes coding for functional proteins essential for the virus' survival. Mutant forms of HIV lacking the *tat* gene appear normal, but are incapable of infecting cells. Moreover, *tat* has been implicated in a variety of the clinical syndromes associated with HIV infection, including fostering the spread of Kaposi's sarcoma and damaging immune functioning. Blocking *tat*'s activity could have several therapeutic benefits.

Roche scientists developed an assay to screen compounds for their ability to prevent the *tat* protein from binding to the viral RNA. To their surprise, the most effective compound they tested was a benzodiazepine derivative, the class of drugs—including the Roche drug Valium—that are used for anti-anxiety therapy. Tests in rats showed that the first candidate drug had unacceptable kidney toxicity, but by the start of this year the company had found a close chemical relative that appeared safe enough to be tested in humans. Moreover, laboratory research showed that the anti-*tat* compound had the added advantage of acting synergistically with drugs like AZT to stop the spread of the viral infection.

News that a trial was imminent first appeared in *AIDS Treatment News*, a newsletter published in San Francisco. The toxicity trial, initially involving about 18 patients, began at Johns Hopkins University in May. But after a few weeks, it was stopped. The reason, according to Roche spokesman Oestreicher, was that the company decided to focus its efforts on two other compounds further along in the drug development pipeline—DDC, a cousin of AZT, and an anti-HIV-protease drug being tested in England. Oestreicher says the decision not to pursue RO 24-7429 does not represent a lack of commitment to AIDS therapies: To the contrary, Oestreicher points out that in addition to the antiviral compounds, Roche is marketing AIDS therapies such as interferon alpha for treating Kaposi's sarcoma

and Bactrim for bacterial infections, as well as new AIDS diagnostic kits for viral detection. RO 24-7429 just didn't fit into the corporate strategy.

But a few weeks after the trial was stopped, the company allowed it to be started again. That decision, according to Oestreicher, came because Roche decided that any company choosing to pursue RO 24-7429 would be able to use the data developed in the trial, and additional toxicity data might make it easier to find a licensee.

Can the government force Roche to pursue RO 24-7429 with greater commitments of human and capital resources? No. But having supported the Roche drug during its initial development, what it can do is "manufacture the drug and evaluate it clinically," says Margaret I. Johnston, chief of the developmental therapeutics branch in the AIDS division of NIAID. But in practical terms, that's just not possible, she says, since the government would have to start from scratch to develop the manufacturing capabilities, using up increasingly scarce resources. Nor can the government require Roche to simply hand over the drug, Johnston says. But were Roche to do so voluntarily, the NIAID AIDS Clinical Trials Group could at least perform the studies necessary to decide whether the drug should be licensed by the Food and Drug Administration. "All they'd have to do really is supply the drug, and they'd get anything that they needed," she says. "The government has the complete resources to develop a drug through additional preclinical studies as well as clinical evaluation."

But Oestreicher says Roche doesn't want to go that route. "Our top-line approach is to identify a corporate licensing partner," he says.

That leaves NIAID with no options but to try to tout the compound in hopes of convincing other pharmaceutical houses to cut a deal with Roche. In that vein, Johnston says: "If I were a company, I would look very seriously at this drug, and working with Hoffmann to develop it." But so far, none have, leaving frustrated federal officials—and of course physicians and AIDS patients—to wait while business strategy determines the future for RO 24-7429.

■ JOSEPH PALCA

The Growing Anti-HIV Armamentarium

By developing a drug that blocks the functioning of the *tat* protein in HIV—a protein that plays a critical role in regulating the expression of viral genes—Hoffmann-La Roche researchers boldly took an entirely new approach from previous efforts to find a chink in the AIDS virus's armor.

The first, and so far most successful, strategy employed by drug companies has been to try to block the action of reverse transcriptase, the enzyme that converts the viral RNA into the host's DNA, sustaining infection. The one antiviral AIDS drug approved so far by the Food and Drug Administration—AZT, manufactured by Burroughs Wellcome—and two similar compounds, DDI and DDC, both nearing FDA approval, all work by this mechanism. But all share a propensity to cause toxic side-effects.

While compounds like AZT and DDI are analogs of the nucleosides that make up the nucleic acids in a cell's nucleus, a second generation of pharmaceuticals are non-nucleoside reverse transcriptase inhibitors. Several—including the TIBO drugs being developed by the Belgian company Janssen Pharmaceutica and BI-RG-587 from Boehringer Ingelheim (*Science*, 7 December, 1990, p. 1411)—are just getting into clinical trials and the good news is that they appear to lack some of the toxic side-effects of the first-generation drugs.

Yet a third promising target for therapy is a viral enzyme called HIV protease, which breaks down a protein made by the AIDS virus into subunits crucial for assembling a mature viral particle. Without a functioning protease enzyme, HIV can enter cells, but can't infect the cells' DNA. Several pharmaceutical manufacturers have focused on antiprotease compounds, since many had already been searching for drugs that work against a similar, naturally occurring enzyme that controls blood pressure. Roche's UK subsidiary was the first to test an antiprotease compound in human patients, but several other companies should begin clinical trials in the near future.

A fourth approach has been pursued by researcher Jeffrey I. Gordon and his colleagues at Washington University. They have found that preventing the addition of myristic acid to key viral proteins is yet another way of blocking HIV infection. Gordon has found several compounds that can rid both chronically and acutely infected cell lines of the virus, but this work is still some way from clinical application.

And then there are the drugs that inhibit the viral spread in the test tube, but for reasons that are a mystery. A compound dubbed "Uniroyal Jr." by researchers at the National Cancer Institute because it comes from the tire manufacturer was discovered in a massive screening program searching compounds that would have activity against the AIDS virus in vitro. Researchers think it blocks some step in the virus's entry into a cell. And Hypericin, now being made synthetically at the Weizmann Institute in Israel, was originally shown to be the ingredient in St.-Johns-Wort that accounted for the plant's antiviral activity. ■ J.P.

ANTIVIRAL AIDS DRUGS IN THE PIPELINE

DRUG	DETAILS	STATUS	DEVELOPER
Nucleoside Reverse Transcriptase Inhibitors			
DDI	Useful alone or with AZT	Nearing approval	Bristol-Myers Squibb
DDC	Combination trials promising	Nearing approval	Hoffmann-La Roche
Fluorothymidine	More potent than AZT, but more toxic	In clinical trials	American Cyanamid
4' Azidothymidine	Longer half-life, less toxic than AZT	Preclinical studies	Syntex
Non-nucleoside Reverse Transcriptase Inhibitors			
L-Drugs	Non-nucleoside RT inhibitor	In clinical trials	Merck
BI-RG-587	Highly potent RT inhibitor	In clinical trials	Boehringer-Ingelheim
TIBO	New version under study in Europe	In clinical trials	Janssen
Protease Inhibitors			
Several candidates	Block virus assembly	Preclinical/early clinical trials	
Myristoylation inhibitors			
Several candidates	Block protein integration	In vitro evaluation	
Other			
"Uniroyal Jr."	Blocks critical stage of infection	Preclinical evaluation	NCI
Hypericin	From St.-John's-wort, blocks RT(?)	Clinical trials imminent	Weizmann Inst.
CD4-PE40	Toxin conjugated with soluble receptor	Preclinical evaluation	Upjohn