French Agency Exonerates Zagury

The storm that has been swirling around AIDS vaccine researcher Daniel Zagury for more than a year may be beginning to clear. A French organization that licenses physicians and oversees medical ethics has rejected a complaint against Zagury from France's minister of health. The complaint, based on the fact that three of Zagury's patients died after receiving an experimental AIDS vaccine he formulated, questioned whether Zagury, an immunologist at the Pierre and Marie Curie University in Paris, had acted in the best interest of his patients. The French licensing body said he had.

In its 3 January decision, a regional branch of the National Medical Order, a nongovernmental body, found that Zagury and his collaborators had "shown a willingness to act openly" by voluntarily clearing their experiments with both the National Ethics Committee and the one at Saint-Antoine Hospital in Paris where Zagury has been conducting his trials of therapeutic vaccines in patients already infected with HIV. The council also concluded that the AIDS patients had been properly informed of the experiment's risks, which were not "out of proportion [to their] state of health and prognosis." Zagury, who could have been barred from practicing medicine if the complaint had been upheld, called the decision "historically important for my family, my research group, my patients, and the scientific community."

The vaccine in question, which Zagury stopped testing after the deaths, was made by isolating white blood cells from each patient and infecting those cells with vaccinia virus that had been genetically engineered to express HIV proteins. Before giving this vaccine to patients, Zagury treated the infected cells with chemicals to kill the vaccinia virus; he added antivaccinia sera to mop up any residual vaccinia particles. More than 20 patients received the vaccine by a slow-drip, intravenous infusion, and no complications occurred. But three died after also receiving either subcutaneous or intramuscular injections of the vaccine. Each developed necrotic lesions at the site of the injections, suggesting that in spite of the precautionary treatments the vaccine contained live vaccinia.

The National Medical Order refused to censure Zagury, noting that the three patients were treated on a "compassionate" basis because they were at a "bad clinical stage" of full-blown AIDS: Each had fewer than 50 T4 cells, critical white blood cells that HIV destroys, when they received the vaccine injections, compared with the normal count of 800-1200. The council stressed that the inactivation methods used by Zagury are widely agreed on in the scientific community and that the necrosis was "not normally predictable, even for confirmed researchers and clinicians."

Supportive as the French licensing body's report is to Zagury, he is not out of the woods yet in France or in the United States. The French minister of health could still appeal the regional branch's decision. And in this country, after *Chicago Tribune* reporter John Crewdson questioned the French researcher's collaborations with Robert Gallo and other National Institutes of Health scientists—and work done by Zagury in Zaire—the NIH Office for Protection from Research Risks (OPRR) issued a stinging interim report in July 1991 criticizing NIH for failing "to provide adequate protection for human research subjects involved in these studies." Zagury, charged OPRR, had violated the collaborative agreement by not promptly notifying OPRR of the deaths in the immunotherapeutic trials. OPRR halted all NIH collaborations with Zagury, although it allowed him to submit new protocols for evaluation. OPRR further recommended that before approving a Zagury collaboration, the NIH must "develop special administrative procedures" to guarantee that patients are protected.

OPRR's plan was to issue a final report based on further information that was to be developed, in part, by the French authorities. Indeed, after the interim report was issued by NIH, the French government had asked Zagury to stop his research in Zaire, where he was testing HIV vaccines in infected and uninfected patients, and formed an official mission to go to Zaire to investigate whether Zagury had breached ethics in his trials there. That mission had intended to visit Zaire in early November but called off its fact-finding trip because of political turmoil in that country. At the time of writing, the French mission had no plans to make the Zaire trip.

Even before the supportive recent verdict, however, Zagury had begun to move forward. With the health minister's approval, he has continued tests of AIDS immunotherapeutics in three patients—although he's now using a different vaccine that is vaccinia-free. Zagury says he hopes to start new vaccine therapy trials this spring with vaccinia-free preparations.

■ JON COHEN

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NSF Under the Magnifying Glass

Investigators on Capitol Hill have been gunning for scandal at the National Science Foundation (NSF) since last August, and NSF director Walter Massey, who is relatively new to the job, sits right where the cross-hairs intersect. This may be why he is sounding jumpy lately: "None of the things that seem to surround other agencies, like internal misconduct or fraud...have come out of this agency," Massey told *Science* last week, yet "we have been subjected to a whole series of inquiries that seem to imply that something is wrong."

The series of investigations Massey refers to began last summer when anonymous informants sent notes to Congress charging NSF staffers were "wiring" contracts (giving them to companies in which they had a financial or personal interest), promoting friends, and shading studies in a way that tended to support NSF's appeal for a bigger budget. The probe gained momentum in August when the House science investigations subcommittee, chaired by Representative Howard Wolpe (D–MI) began asking questions of the NSF staff. He wasn't satisfied with the first batch of answers he got, and the inquiry continues, focusing on two areas: The NSF's Division of Science Resources Studies (SRS), which publishes data on the R&D workforce and the financial support of science and technology, and on what used to be called the Division of Policy Research and Analysis.

Neither Massey nor his predecessor Erich Bloch would claim there were no problems in these two offices. According to *Science and Government Report*, Bloch had warned Massey at the time he turned over the directorship that dangers lurked—especially in the SRS division. Under Massey, both offices were reorganized. Furthermore, Massey points out, the SRS division has undergone several close examinations in the past year. The U.S. Office of Government Ethics took a look, as did NSF's inspector general, Linda Sundro. She concluded in a report issued in December that the investigation turned up nothing criminal—no "actionable findings of bias" or unacceptable conduct—just "a pattern of mismanagement and poor contracting practices."

More esoteric than the contract inquiry—but potentially just as embarrassing for NSF—is the investigation into what is being called the "pipeline paper," a series of analyses by

the policy office describing the flow of scientists and engineers through the educational pipeline. At issue is a policy analysis widely cited by former NSF chief Bloch and other NSF staffers during their campaign to win a bigger NSF budget from presidents Reagan and Bush. Critics have questioned the credibility of the analysis.

These studies were prepared under Peter House, then director of the Division of Policy Research and Analysis. They predicted that the United States would experience a "shortfall" of technical expertise at the end of the century unless steps were taken quickly to increase the number of students receiving bachelor of science and Ph.D. degrees. House was so proud of this work that he took credit, as reported by Jeffrey Mervis in *The Scientist* last October, for publicizing a forecast that he claimed "helped to justify President Reagan's proposal to double the NSF budget over 5 years."

House's analysis since then has run into harsh criticism from economists and labor statisticians who fault its methodology. One early skeptic, Alan Fechter, a director of the National Research Council's office of scientific and engineering personnel, wrote that the studies differed from most economic analyses because they did not consider possible changes in demand. The result, Fechter claimed, is that the NSF created a theoretical (but unsubstantiated) specter of a "shortfall" in the supply of researchers by the end of the century—one that would disappear if different demand assumptions were used. This analysis, Fechter wrote, was "not very useful for policy formulation," though it clearly was useful for NSF officials seeking a bigger budget.

Massey told *Science* last week that the investigation into these matters is "a distraction" for the staff. It's a distraction he professes to be baffled by, since NSF sleuths have probed some of the same issues and failed to dig up any violations of law or significant procedural abuses. "I just have no idea what the motivation" for the inquiry is, says Massey. The mood on Capitol Hill is quite different. Indeed, the picture one aide painted is that of NSF officials flipping out over what is nothing more than a standard oversight inquiry.

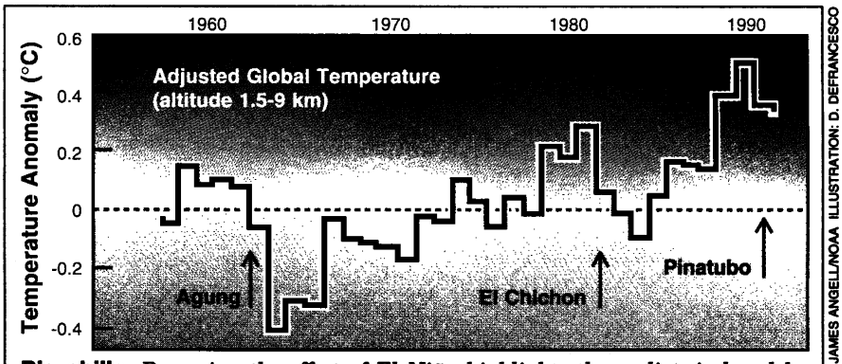
Those opposed viewpoints are also reflected in what various parties think the outcome of the current investigation is likely to be. NSF staffer Joel Widder says he thinks the dispute over the pipeline paper is just a case of "policy analysts chewing each other alive." Wolpe's staff clearly disagrees. The investigation is expected to grind on for 2 or 3 months before the public finds out how Capitol Hill interprets the goings on at NSF.

■ JOSEPH PALCA and ELIOT MARSHALL

1991: Warmth, Chill May Follow

Earth was still running a fever in 1991, but relief, albeit temporary, may be here. Following on the heels of 1990's record temperatures, last year ended as the second warmest ever recorded. But it might have set yet another record had it not been for the eruption of Mount Pinatubo. The layer of sun-blocking haze spewed by the Philippine volcano is sending a chill through the climate system that may already have shown up in the temperature record.

This volcanic cooling, which could last a couple of years, should also temporarily chill the debate about whether the greenhouse effect is behind the warming of recent years. It's been hard enough to draw firm conclusions about any greenhouse warming from world temperature data, and Pinatubo's masking effect should make it harder still during the next few years. But the cooling episode may advance the science of climate prediction indirectly. It will give scientists an opportunity to check out their computer greenhouse models by seeing how well they do at predicting the volcano-induced climate change. The stakes are high, says modeler James Hansen of NASA's Goddard Institute of Space Studies (GISS): "Either we're going to see a [temperature] signal, or [our] model is wrong."



SOURCE: JAMES ANGELL/NOAA ILLUSTRATION: D. DEFRANCESCO

Big chills. *Removing the effect of El Niño highlights the cooling induced by volcanic eruptions. (Last year was the fourth warmest in this tropospheric record.)*

If the model is right, a long-term warming trend is due for a reversal. Helene Wilson of GISS and Hansen note that the 8 warmest years in their 110-year record of land surface temperature all occur within the past 12 years. And the warming of the past 25 years has been more rapid than during any comparable period in the record.

Last year the heat stayed on. All three groups compiling global surface temperature observations—GISS, NOAA's Climate Analysis Center, and a joint effort by the British Meteorological Office and the University of East Anglia—pegged last year's global temperature at just below the record warmth of 1990. The continued heat wave may have been bolstered by the unusually warm waters that collected in the western tropical Pacific, points out climatologist James Angell of NOAA in Silver Spring, Maryland. The Pacific warming began more than a year ago, even though it was not until last fall that it became extensive enough to trigger a full-blown El Niño—the warming of the tropical Pacific that is already bringing floods to Texas and unseasonably mild temperatures to the northern tier of states.

Can the El Niño overcome Pinatubo's cooling effect during 1992? Climatologists say the odds are against it. Even a strong El Niño warms the globe by only 0.1 to 0.2°C, while Hansen's computer model predicts that the debris lofted into the stratosphere by Pinatubo should block enough sunlight to cool the world by about 0.5°C, an amount equal to all the warming of the past 100 years. "It's not clear the man in the street will see the signal so clearly," says Hansen, "but it's a nice model test."

If the world cools less than predicted, for example, it might be because the system is less sensitive to climatic influences than has been assumed. Greenhouse warming might then fall short of the potentially disastrous heating that many models now predict. It's too early to say how well the GISS prediction is holding up, but by year's end the GISS record shows that the global temperature curve had edged downward by several tenths of a degree. Check these pages this time next year to see how the models, and Earth, are faring.

■ RICHARD A. KERR