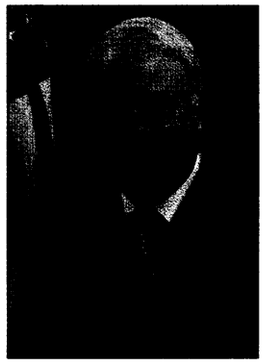
HIGH-ENERGY PHYSICS

Peña to Review LHC Agreement

The U.S. government plans to review its tentative agreement with Europe to help build the Large Hadron Collider (LHC), to make sure it is a good deal for this country. The review, announced last week by Energy Secretary Federico Peña, comes at the urging of Representative James Sensenbrenner (R–WI), who chairs the House Science Committee. Agency officials say they are confident that most of the lawmaker's concerns can be met with only minor changes to the proposed partnership, while European managers insist that the current agreement already addresses most of Sensenbrenner's worries.

Department of Energy (DOE) officials hope to provide $450 million worth of hardware for the accelerator and its two main detectors, with the National Science Foundation chipping in an additional $80 million for the detectors. The LHC, with a total budget of $5 billion, is slated for completion in 2005 at CERN in Geneva; DOE and CERN managers signed a draft agreement in February spelling out U.S. and European responsibilities. But some House members, including Sensenbrenner, think the United States is getting a raw deal, and the House Science Committee has denied specific funding for the project in the 1998 DOE authorization bill. The bill should reach the House floor next week.

Skeptics in Congress harbor deep resentment toward Europe's perceived indifference to the fate of the Superconducting Super Collider (SSC), which was voted down by Congress in 1993. Last week, at a colloquium sponsored by the American Association for the Advancement of Science (AAAS, which publishes *Science*), Sensenbrenner accused CERN officials of having "raised an upright finger" at U.S. requests for financial backing for the SSC. His main concern now is that the United States lacks an adequate management role in the LHC and that cost overruns could lead to requests for additional U.S. funds. He also wants a contractual agreement to ensure U.S. access to the complex and a pledge of financial support from European science managers for any future accelerator in the United States, in return for U.S. help with the LHC. Finally, House staffers say the committee chair would like CERN to revise procurement practices that he believes discourage the purchase of U.S. goods.



Colliding views. Rep. Sensenbrenner wants U.S. to rethink its agreement with CERN on the LHC.

"The answers to all his questions are in the agreement we negotiated," says Christopher Llewellyn Smith, CERN's director-general. "It is a mutually very beneficial deal, and I think that with explanation and time, Congress will understand it is a good deal." As a CERN observer, Llewellyn Smith says, the United States will have a forum to express its concerns. CERN already has a written open-access policy for non-European researchers, he notes, and the LHC agreement includes further assurances. As for unexpected costs, he says, "we think the chance of overrun is very small" given that the device is being built in an existing tunnel.

Sensenbrenner met with Peña on 23 April; 2 days later, at the AAAS colloquium, Peña said that some of the chair's concerns are legitimate. Saying that he is willing to "go back and make some changes," Peña noted that some revisions may not require action by the full CERN council. Other Administration officials agree with Llewellyn Smith's overall assessment about access and costs, and they are loath to demand a larger U.S. management role. "We don't want to be a CERN member," says one official. "That would be too expensive."

–Andrew Lawler

With reporting by Alexander Hellemans in Paris.

SCIENCE AND COMMERCE

Disclosing Data Can Get You in Trouble

Even if you hold no stock in a company sponsoring your research, you can get yourself into serious legal trouble if you speak too freely—even to your spouse—about results that could affect the company's stock price. Milton Mutchnick is learning that the hard way. On 10 April, the U.S. Securities and Exchange Commission (SEC) filed insider-dealing charges against Mutchnick, a gastroenterologist and well-known expert in liver diseases at Wayne State University School of Medicine in Detroit, along with his former assistant, Rangarao Panguluri. The SEC has accused them of illegally disclosing early, negative results in a clinical trial of a hepatitis-B drug (thymosin alpha 1), allowing friends and relatives to beat the market by selling off stocks.

The SEC's associate director of enforcement, Thomas Newkirk, says this is the first insider-trading case the SEC has brought against clinical researchers. He claims that the "tippees" who received the early information from Mutchnick and Panguluri in 1994 avoided financial losses by quickly selling stock in two companies—Alpha 1 Biomedicals of Bethesda, Maryland, which sponsored the trial Mutchnick supervised, and SciClone Pharmaceuticals Inc., of San Mateo, California, which had bought the rights to market thymosin alpha 1 overseas. Three days after the clinical results were leaked in April 1994, Alpha 1 Biomedicals issued a press release saying that the clinical data would not support an application to market the drug in the United States, and it abandoned the project. SciClone's stock also took a hit, but the company didn't give up. Under drug-export rules that Congress simplified in 1996, it has been selling thymosin alpha 1 in China for hepatitis B and other infections. And the company announced this year that it plans to market the drug in at least 25 foreign countries.

Panguluri, now a physician in private practice in Anaheim, California, is contesting the SEC charges. Neither he nor his attorney responded to phone messages left at their offices. Mutchnick agreed to a judgment last month that requires him to pay the government $163,494.75—a fine equivalent to the stock losses the SEC claims his friends and relatives avoided because they got access to inside information. The judgment, in which Mutchnick neither admits nor denies the SEC's charges, also compels him to avoid speaking against the agreement.

Mutchnick thought he and his colleagues had insulated themselves from potential conflicts of interest when they ran the clinical trial of thymosin—the first major test of the drug. "None of the investigators [in the thymosin trial] held stock" in companies backing the drug, Mutchnick says, adding, "I thought that gave immunity" to conflict-of-interest and insider-trading charges. But, in this case, the researchers are charged with violating a section of the 1934 Securities Exchange Act by "disclosing or misappropriating ... material, nonpublic information concerning the Phase III trial of thymosin."

Mutchnick, noting that the experience has been "very hurtful," claims he got into trouble in part through "my own naiveté." As the principal investigator, he says, "it never occurred to me that I couldn't talk about my impressions" of how the trial was going. Mutchnick was both principal investigator and, during years of tox-

icity testing, holder of the investigational new drug (IND) permit, which gave him a sense of ownership of the data, he says. In the final year of the phase III trial, which tested for efficacy, Mutchnick turned the IND over to Alpha 1 Biomedicals, he says, because he "couldn't handle all the paperwork." But he continued to discuss the trial.

He also met with stock analysts and investors, at Alpha 1's behest and expense, to talk about the progress of the trial. (Indeed, after the stock plummeted in 1994, a group of investors sued Alpha 1, claiming Mutchnick and the company had exaggerated the drug's value; the plaintiffs eventually settled out of court.) These meetings, which the SEC did not challenge, gave Mutchnick the idea that it was all right to share information about the clinical trial with other interested third parties, he says. Besides, he argues, a scientist must speak openly about his research: "I've never said 'No comment' in my life. ... I couldn't say 'No comment' for 5 months, " while waiting for the company to decide what the data signified and make a public announcement.

According to the SEC complaint, Mutchnick and Panguluri unblinded the data on patients receiving a placebo or thymosin at about 3 p.m. on 25 April 1994. They found "an equal response rate across both groups with respect to the disappearance of viral DNA," the SEC says, a strong indication "that the study had failed to demonstrate thymosin to be effective in the treatment of hepatitis B." The SEC alleges that Mutchnick visited his sister and brother-in-law at 7 p.m. and told them the bad news. Before the stock market opened the next morning, the SEC charges, his brother-in-law had placed an order to sell stock in Alpha 1 Biomedicals and SciClone Pharmaceuticals.

The SEC even takes Mutchnick to task for sharing the bad news with his wife, Renee, claiming that Mutchnick "knew, or should have known, or acted with reckless disregard of the fact, that Renee Mutchnick was likely to disclose the information to others. ..." The Mutchnicks, according to the judgment, spread the news to three friends and to Renee's father and sister, all of whom sold stock the next day or the day after. The SEC also alleges that Panguluri tipped off two doctors in the Anaheim medical practice he was negotiating to join, and that they and their friends quickly dumped stock. On 28 April 1994, Alpha 1—pressured by a massive sell-off of stock—issued a press release disclosing the negative results of the clinical trial.

Today, Mutchnick says his initial impression of the trial results was hasty and erroneous, and he believes that thymosin alpha 1 was "defamed" by the "premature" press release of 28 April. He claims that on reanalysis, his own clinical data show that the drug is useful in treating hepatitis B. Some of the data were presented at a meeting in 1995, but have not been published as yet. Another study of 33 patients based in Bologna, Italy, published in 1996, found that thymosin alpha 1 was better than interferon α in controlling hepatitis-B infection. And several other foreign studies (not yet published) indicate—according to SciClone—that thymosin is effective for controlling hepatitis B and C.

SciClone's chief financial officer, Mark Culhane, says the company did a meta-analysis of data from these studies to support its application to foreign health authorities to sell thymosin, under the name Zadaxin, in China and the Philippines. It is already planning to market thymosin in Singapore and Taiwan. For Culhane, the logic of the marketplace may be more germane than lingering quibbles about the clinical data: He notes that thymosin "is being sold" right now, "which is the ultimate confirmation" of its value. SciClone, unlike Mutchnick, may yet profit from the drug.

–Eliot Marshall

AIDS RESEARCH

Montagnier to Head New York Center

PARIS—Luc Montagnier, whose group here at the Pasteur Institute first isolated HIV in 1983, surprised the world of AIDS research last week by revealing that he intends to team up with an American entrepreneur to create a new research institute in cell and molecular biology—focusing principally on AIDS. The new institute will be at Queens College in Flushing, part of the City University of New York. Montagnier, who has just completed a 6-year term as head of the Pasteur's AIDS and retrovirus research department, will maintain his own laboratory at the Pasteur Institute and will continue to work with two organizations he co-founded: the World Foundation for AIDS Research and Prevention, and the Luc Montagnier Center, an AIDS research institute in Paris.

REMY DE LA MAUVINIERE/AP

On the move. HIV co-discoverer Luc Montagnier.

Some AIDS specialists wonder how much Montagnier will be able to achieve in the United States with so many other demands on his time. "It's not clear what he can do there that is not already being done," says a colleague at Pasteur who asked not to be identified. The 64-year-old Montagnier—who is nearing retirement at Pasteur—is "already running three other operations at once. He may not be able to keep up," the researcher says. Montagnier told *Science* he plans to commit "a large part" of his time to Queens College. (According to sources at Pasteur, Montagnier will be replaced as head of the AIDS and retrovirus department by hepatitis-B expert Pierre Tiollais.)

Montagnier was lured to Queens by college alumnus Bernard Salick, former chief executive of Salick Health Care, a chain of 24-hour cancer-care and kidney-dialysis outpatient clinics. Salick was ousted as CEO of the chain earlier this month, after a takeover by the British pharmaceuticals giant Zeneca, but he is donating $4.5 million of his own money to start the center. In addition, Salick and Queens officials will attempt to raise some $15 million from the state of New York and matching funds from private sources. "The outlook is very good," says Queens spokesperson Ron Cannava, "because Salick has tremendous contacts with the pharmaceutical industry."

According to Montagnier, the center will hire five prominent researchers, who will be appointed senior-level professors at Queens College. Montagnier says that the center's AIDS research will be focused primarily on finding therapies "that would relieve patients from having to be treated every day for the rest of their lives," as well as development of an AIDS vaccine. Although some researchers from his Pasteur lab or the international network of researchers supported by his foundation may move to the new institute, Montagnier says that "it will be mostly an American center, run by Americans." Montagnier adds that he has already begun sounding out some U.S. scientists about coming to Queens, although he declines to give names at this point.

The new institute will take about 2 years to construct. But Montagnier says he is eager to begin work as soon as he can negotiate temporary lab space at Queens. Asked what attracted him to set up shop across the Atlantic, Montagnier says that in the United States, research discoveries can be exploited much more rapidly than in France: "There is a greater potential for having findings applied by industry and biotechnology companies, and more opportunity to interact with those groups."

–Michael Balter