about whether to give TPA to patients. We're asking what do we do after we give TPA."

Eugene Passamani, associate director of the heart institute and director of its TPA trials, and Braunwald each say that a mortality study involving TPA would be difficult to conduct because it would require thousands of patients. In their opinion, the mortality studies involving streptokinase should be sufficient evidence that a clot-lysing drug helps patients. A mortality study comparing TPA against a placebo would now be "unethical," Braunwald adds. European researchers have conducted a study comparing TPA and a placebo and reported no difference in mortality. But Braunwald says that the study, which involved about 120 patients, was far too small to measure a difference.

FDA officials concede that the agency never specifically requested mortality data from Genentech until shortly before the meeting. By then it was clearly too late to generate that kind of data. In fact, in 1984, an advisory panel to the Office of Biologics Research and Review said that mortality studies would be "so experimentally demanding that they would not yield useful data in the near future." Peter Drake, an analyst at Kidder Peabody, says, "FDA changed the rules and the playing field in the eighth inning."

The rules might have been changed because a regulatory turf battle between two branches of FDA broke out, Drake and others assert. But the reasons could stem simply from bureaucratic inefficiency as well. Since 1984, FDA's Office of Biologics Research and Review has informally discussed with Genentech the clinical data that the company should consider providing before it actually submits an application for product approval. This is not an uncommon practice because human studies can take a long time to design and conduct.

About a year ago, Genentech applied for approval from the biologics office. In December, director of the biologics office Elaine Esber asked the Office of Drug Research and Review, headed by Temple, to examine the application, a move which ultimately led to the advisory committee's review of the drug in May. Temple's branch is responsible for the review of synthetic pharmaceuticals, including heart drugs. Shortly afterwards, officials from that branch fired off a long list of questions to Genentech. Then the cardio-renal advisory committee, which reports to Temple's branch, was requested to review the application. When asked why Temple's office was not brought in formally earlier in the process, officials in the biologics branch say that Genentech made its application a year ago, which they consider a short time ago. And they add that informal discussion about the application has been held in the hallway. A former FDA official involved in TPA's review, who criticizes the way FDA handled the Genentech application, said, "Intelligent people can disagree from day one, but not late in the game."

FDA is not bound by the committee's recommendation, but it would be highly unusual if the agency went against it. Data from the current Johns Hopkins trial that is testing TPA's effect on heart function and from the heart institute's ongoing study may be enough to satisfy the agency's concerns. Since the committee meeting, Genentech officials have met once with FDA staff and once with FDA commissioner Frank Young, who has tried to accelerate the approval process for drugs. Analysts are betting that TPA won't be approved for another 6 to 18 months.

Braunwald says, "There are so many interests in TPA, in turf, dollars, and principle. But the most important concern is the patient. What I'd like to see is some meeting of the minds. I'm not saying TPA is the only way to achieve it [clot lysis], but it's a terrific way to do it." ■ MARJORIE SUN

U.S. Policy on Exchanges with the Soviets Called a "Shambles"

"In my view, the process by which decisions are made that affect broad policy, detailed negotiations, and eventual implementation of agreements for scientific and technical exchanges with the Soviet Union is a shambles, marked by indifference, incompetence, and parochialism." That's the opinion of Richard Perle, former assistant secretary of defense and currently resident scholar at the American Enterprise Institute. Perle was the lead-off witness for 2 days of hearings on U.S.–Soviet scientific exchanges, held by the new House subcommittee on international scientific cooperation.

Never one to mince words, Perle accused the State Department's Bureau of Oceans, International Environmental and Scientific Affairs of succumbing to "reckless abandon . . . whenever it encounters a Soviet scientist with a pen in his hand" ready to sign a scientific agreement. Perle, who spent a lot of time when he was in the government arguing against broadening scientific contacts with the Soviets, said that the Soviet Union routinely gains the lion's share of benefits from exchanges, and he expressed astonishment that U.S. government agencies would advocate extending and initiating exchanges with the Soviet Academy of Sciences, "an organization known to be part of the Soviet intelligence establishment."

Two days later, John Negroponte, who heads the State Department's scientific bureau, delivered himself of a measured review of U.S.–Soviet exchanges over the years, ticking off a list of benefits. "It would be short-sighted of us not to recognize that it is in our national interest to seek to expand scientific cooperation with the Soviet Union. We have gained much from this relationship already," he said.

Perle and Negroponte clearly reflected opposite poles of a debate that has been going on within the Administration for the past 6 years. Their appearances provided good theater, but little more, however.

Perle, for example, said "the unhappy fact is that we have no policy, no deliberate sense of gains and losses, no orderly interagency process for evaluating risks and benefits. We have been operating on a chaotic, case-by-case adhockery that reflects the careless indifference with which policy levels in the executive branch have treated the whole subject."

"I simply cannot agree," countered Negroponte, who pointed out that the State Department produces an annual report, called "Science, Technology, and American Diplomacy," which includes a "systematic evaluation" of science and technology agreements.

The hearings were held in part to probe into two recent incidents in which the Defense Department was instrumental in blocking agreements involving the Soviets. These were a decision by the National Security Council (NSC) to instruct the National Science Foundation not to fund a grant to the International Institute for Applied Systems Analysis, an East-West think tank based in Austria, and a second NSC directive to disinvite the Soviets from joining the international Ocean Drilling Program. In both cases, Perle's office had objected, but the reasons have never been spelled out in public.

The hearings shed little new light on the incidents, however. Perle, it seems, had simply won another round in the political battles between Defense and State. ■

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