strategies while those who understand technology are in such a peripheral status."

Part of the problem seems to be that economists have had great difficulty in finding a compatible and efficient way to handle the technological factor. As a result, writes Raymond Vernon, professor of international trade and investment at Harvard University, economists "have been slow to incorporate that [technological] variable explicitly in the main body of trade theory."

One of the few economists who seems to have looked closely at Boretsky's data is Richard Nelson, professor of economics at Yale, who has done pioneering work in the economics of research and technology and who sits on Haggerty's PSAC panel. "I'm basically with Boretsky," Nelson told *Science*. "I think the argument is almost unassailable." Nelson said he agrees that an erosion of U.S. technological leadership is the key factor behind trade balance problems, but he seems somewhat less worried about the situation than is Boretsky. "Boretsky waves his arms and screams too much," Nelson said. "I'm quite worried about his alarmist tone. It may force us to do silly things." Nevertheless, Nelson credits Boretsky (who is not widely known in the economics community) with making "a major contribution" by pulling together and analyzing data that no one else seems to have studied. Nelson said that while a handful of economists have, for the past decade or so, been studying the impact of technology on international trade, their work is still only trickling into the main line literature. "I don't feel my confreres realize how important it [technology] is," Nelson says. "It's very important."

—PHILIP M. BOFFEY

Food and Drug Administration: Is Protecting Lives the Priority?

In January officials of the Food and Drug Administration (FDA) knew that the use of bottled intravenous feeding solutions manufactured by Abbott Laboratories had somehow led to an outbreak of blood poisoning and several deaths. Yet they took no action. In early March, the FDA found out that a large percentage of the Abbott solutions were contaminated with the infectious bacteria responsible for the blood poisoning. Yet they did not ban the products. They only recommended that certain precautions be taken when the solutions were given to patients. Not until 22 March did FDA recommend that hospitals stop using the Abbott products. And then only after consumer-advocate Ralph Nader appeared on national television denouncing the agency for its failure to act.

The intravenous (I.V.) solutions (mostly combinations of dextrose and salts in water) are used in virtually every hospital to feed nutrients to critically ill patients. Until the ban Abbott Laboratories supplied 45 percent of the 250,000 bottles of I.V. solutions administered daily to patients in the United States.

The magnitude of the epidemic brought on by the Abbott products is unknown. The federal Center for Disease Control in Atlanta (CDC) carefully documented 150 cases of blood poisoning including nine deaths in only eight hospitals. But over 8000 hospitals were using the Abbott products at the time the contamination was discovered. A spokesman for CDC told *Science*, "We have no way of knowing the full extent of the problem, but you can extrapolate a guess."

A decision by FDA officials to ban any product involves complex consideration, many of them subjective. And from the vantage point of hindsight, the FDA can make an easy target for critics. Nevertheless, the case of the Abbott's I.V. solutions involved enough irregularities and a sufficient number of deaths to warrant close scrutiny. Whether or not anyone acted incorrectly, the incident is likely to result in congressional hearings and another round of criticism of the FDA.

Included among the irregularities is a curious history of violations involving Abbott's I.V. solutions, none of them resulting in prosecution by the FDA. In 1969, FDA inspectors found hairline cracks in some bottles of the Abbott solutions, which resulted in contamination. Abbott agreed to recall the damaged bottles and improve its manufacturing techniques. In 1964, FDA first cited Abbott several times for mislabeling its I.V. solutions, then, later in the year, because two lots were discovered to be moldy, and finally because the caps on the bottles were shown to leak.

The House Intergovernmental Relations Subcommittee, while investigating the 1964 series of violations, discovered that high FDA officials in Washington had suddenly ordered an end to the investigation of Abbott Laboratories. During an inspection of Abbott's plant in North Chicago, two FDA field inspectors received a phone call from their superior ordering them to "get out of the plant by noon." The investigation was thus precipitously concluded. And no satisfactory explanation has been offered.

The death of a 28-year-old woman on 5 July 1970 at the Medical College of Virginia in Richmond called the first attention to the current problem. Although hospitalized for hepatitis, the woman died from blood poisoning (septicemia). And the same rare bacteria found in her blood were growing in her bedside I.V. feeding bottle. Richard J. Duma of the college's department of internal medicine, while investigating the death, found that two other patients had recently contracted blood poisoning from the same organism. Duma and two colleagues, John F. Warner and Harry P. Dalton, then sampled all of the I.V. units in use in the hospital. Thirty-five percent of the solution bottles were contaminated with the same organism. The hospital's entire supply was manufactured by Abbott. "I had a lot of trouble getting people to believe that so many of the bottles were contaminated," recalled Duma.

Despite the extent of the problem, unopened bottles of the I.V. solutions showed no signs of contamination. "We concluded that the source of the contamination was at the bottle cap," said Duma. "But we were unable to tell

whether the bacteria were coming from the manufacturer or getting into the bottles after they were opened."

As soon as he was sure of his results (in late July), Duma notified FDA, CDC, and Abbott. CDC, the Public Health Service unit responsible for monitoring outbreaks of infectious disease, immediately dispatched a representative to the hospitals. Pending the investigation by CDC, FDA took no action. And Abbott only replied that the product was manufactured with adequate quality control. Meanwhile, Duma concluded that he had best get his results published in order to alert others to the potential danger. Duma's findings appeared in the 4 February issue of the *New England Journal of Medicine* (**285**, 257).

In early December, three CDC investigators, Dennis Maki, Conrad Fulkerson, and Frank Rhame, began a thorough study of the epidemic in the Virginia hospital. At first they assumed that the contamination originated outside of the bottled solutions. Accompanying the bottled solutions are disposable kits to deliver the liquid slowly into the patients' veins. And contamination could enter the system from the air or from a nurse's hand as she sets up the apparatus.

"We had regarded the prepackaged sterilized products as inviolate," said Fulkerson, "particularly since the unopened bottles showed no contamination." Thus they searched, with no luck, for some source of the bacteria in the hospital.

Nationwide Epidemic

Late in December, however, the CDC investigators discovered that the problem went beyond the Virginia hospital. Through a chance conversation with a friend in California, Maki learned that a similar outbreak of blood poisoning with the same rare bacteria had occurred at Orange County Hospital. Then on 5 January, St. Anthony's Hospital in Denver reported 24 cases of blood poisoning and one death, again from blood poisoning due to the same organisms. Later in the month, Henry Ford Hospital in Detroit reported 45 cases and eight deaths.

Since the Medical College of Virginia used the Abbott products exclusively, no evidence had conclusively linked the Abbott solutions and the infections. But each of the newly discovered outbreaks involved the Abbott I.V. solutions. Furthermore, the CDC investigators had "cultured out" the I.V. solutions at a hospital that didn't use Abbott and found no contamination or infection. Thus, while they still didn't know how it was happening, the investigators realized that something about the Abbott products was resulting in blood poisoning. "Epidemiologically, it was damned suspicious," said Maki.

The decision to remove a product from use rests not with CDC, but with the FDA. All through the investigation, George Blatt of FDA's Office of Compliance kept tabs on the CDC findings. Blatt does not believe that the relation discovered in January between the disease and the Abbott products warranted any action by the FDA and, indeed, FDA did nothing at the time.

"You don't take legal action against a firm," Blatt told *Science*, "until you have evidence that can stand up in court. You have to define where the problem is. And all you had at the time was an association of the disease with the product." He emphasized, however, that the decisions regarding action against Abbott were made not by him, but by the Commissioner of Food and Drugs, Charles E. Edwards.

But, in spite of the illnesses and deaths resulting from the products, Edwards says he knew nothing of the problem. In an interview with *Science*, both Edwards and his associate commissioner for compliance, Sam Fine, insisted that the first they heard of the difficulties, other than what had been published in the *New England Journal of Medicine* was 11 March. That was after the discovery of the contaminated bottle caps.

Blatt told *Science*, however, that "Of course, Fine and Edwards knew of the investigation all along." But when told that they denied knowing about it, he replied, "I report things and I write memos. But someone above me makes the decisions about who sees them."

In any event, immediate action became imperative with the discovery of the guilty germs in a space between a plastic liner and an aluminum disk in the Abbott solution's bottle cap assembly. By 10 March, the CDC investigators were convinced that a certain portion of the Abbott I.V. fluids had left the factory contaminated. They surmised that the bacteria escaped into the solution if the bottle was shaken so that the fluid washed over the bottle cap liners.

On 11 March representatives of Abbott, FDA, and CDC met in Atlanta. The next morning David Sensor, the director of CDC, Edward J. Ledder, the president of Abbott Laboratories, Surgeon General Jesse Steinfeld, and Commissioner Edwards met in Washington to discuss the problem. That afternoon Edwards and Sensor announced at a press conference that a ban was not feasible and that "special precautions must be taken . . . to reduce the risk of septicemia from the use of Abbott Laboratories' intravenous infusion products." The precautions included gentle removal of the bottle caps, changing of the I.V. apparatus every 24 hours, and watching for the first signs of blood poisoning.

They also announced that "these products will be replaced as rapidly as possible by Abbott." A spokesman for the FDA insisted that Abbott representatives at the meetings came only to supply information and had nothing to do with the decision.

Shortage of Alternate Supplies

In explaining his decision on 13 March not to ban the use of the contaminated solutions, Edwards told *Science*, "You've got to understand that all we had at that time was very preliminary data. We believed that the precautions could allow the solutions to be used safely." Edwards also emphasized that FDA didn't have accurate information about the availability of replacement products from Abbott's competitors. And since Abbott was supplying 45 percent of the critical solutions, he could not simply order hospitals to stop using the Abbott products. "We might have killed more people by banning the Abbott solutions than by allowing their use," added Fine.

Yet FDA officials acknowledge that they did not even check on the availability of solutions from other manufacturers until after the 13 March announcement. Thus while FDA met with Abbott on 12 and 13 March, Abbott's three competitors, Baxter Laboratories, Cutter Laboratories, and American Hospital Supply, heard from FDA a few days later. When on 19 March government specialists did complete a survey of the competitors, they concluded that, for the most part, hospitals' stocks of Abbott solutions could be replaced. "The reason for the delay," said Edwards, "was that we didn't know of the problem until 11 March. After that we acted as fast as possible."

Although the FDA had declared that the Abbott solutions could be used safely, the Army disagreed. On 15 March, the Army Surgeon General issued a

worldwide notice ordering all Army medical facilities "to suspend from immediate use and issue all Abbott intravenous solutions." The Army and the FDA differed in their actions, according to one medical officer, because the Army wasn't depending solely on Abbott products. And "because in the military services we never take a chance with a product that might be faulty."

On 19 March, Sidney Wolfe, a Washington internist and member of the Medical Committee for Human Rights, heard from a physician friend in New York. Wolfe's friend claimed that the extent of the infections caused by the Abbott solutions in his hospital exceeded the number claimed by government officials. He also claimed that the FDA-recommended precautions did little to reduce the incidence of blood poisoning.

After investigating the problem, Wolfe contacted Ralph Nader, who agreed to send a joint letter to Edwards demanding a ban on the product. The letter sent the following Sunday (21 March) alleged that ". . . there is a clear mandate from the data the CDC has collected to order Abbott intravenous products off the market and thereby *insure* the end of this epidemic of blood infections and death."

Nader and Wolfe were particularly critical of one of the FDA precautions that read: "At the first suspicion of septicemia which might be associated with contaminated intravenous fluid, all existent IV apparatus should be removed. . . ." Claiming that "it is a form of malpractice to wait until a patient develops evidence of the blood infection," the letter said, "the recommendation is a cowardly repudiation of the ethic of preventive medicine."

In response to an appearance on national television news by Nader and Wolfe publicizing their letter, Edwards defended his 13 March decision. But the next day he essentially followed their recommendation and banned the use of all Abbott I.V. solutions, except for emergency situations.

Listing the reasons for the change of decision, Edwards included new evidence regarding the extent of the epidemic, availability of alternative suppliers, and the ease by which bacteria can find their way into the I.V. solution. After 13 March, while evidence of new cases of blood poisoning was pouring into CDC headquarters, the three investigators who had located the contamination were working 20 hours a day trying to find the mechanism of the contamination. They found that one need only twist the cap, not shake the bottle as they had thought, to release the bacteria. Thus they concluded that the Abbott solutions were unsafe under any conditions.

Abbott Laboratories issued a press release stating that "it will co-operate with the FDA" and emphasizing that the I.V. solutions represented only 8 percent of the company's total sales last year. Beyond that, however, company officials refuse to discuss the matter.

Even though all the pieces of the puzzle weren't in place until the third week in March, FDA officials clearly had sufficient information to take action and save lives before then. One might ask why FDA officials believe that a strong association between a product and a serious infection is insufficient reason to take action against the product. Or, why, at the very least, they had not investigated the availability of alternative supplies of the I.V. solutions at the first suspicion of the Abbott products.

Only a congressional investigation can provide the answer to those questions, since FDA tends to regard the specifics of its regulatory decisions as privileged information.

—ROBERT J. BAZELL

Research Grants: New Awards Bore Brunt of NIH Cutbacks

Measuring the breadth and depth of the current recession in federal support for science and its impact on the conduct of basic research has proved to be a baffling task at best. Even now, as the budgets of some major federal research agencies creep upward again, there remains a dearth of "hard," quantitative information about the financial health of American science—even from the agencies themselves.

For the most part, the recession in sciences remains evident chiefly in terms of anguished anecdotes from the nation's campuses telling of curtailed research and discouraged graduates. But anecdotes have a way of sounding very much like special pleading, especially when contrasted with seemingly small cuts in the overall budgets of research agencies. As a result, they have provided only a poor composite picture of the fiscal situation.

In the partial vacuum of objective information, however, a small unpublished study by an ad hoc committee of the National Academy of Sciences appears to provide a fresh and important new glimpse into the making of the research slump.

Conducted last year, the study focused on the National Institutes of Health (NIH) and its support for new research and grant renewals, particulary in chemistry. The study shows in great statistical detail that money for these purposes from the various institutes declined by an average of 20 percent, and that the NIH unit with perhaps the deepest commitment to basic research—the National Institute of General Medical Sciences (NIGMS)—lost fully half of its money for new research and renewals in 1970. The study indicates that such a sharp decline, coupled with termination last June of the NIH predoctoral fellowship program, understandably traumatized the research community. And in important ways the study helps to reconcile the anecdotes with the budgets.

The five-man committee* which conducted the inquiry was headed by Virgil Boekelheide, a professor of chemistry at the University of Oregon and chairman of the National Research Council's division of chemistry and chemical technology. Although results of the study have not been published yet, a few copies of data which the NIH gave to the committee and a summary statement are circulating around Washington. And some top

* Other members were Ronald Breslow, Columbia University; John D. Roberts, California Institute of Technology; Henry Taube, Stanford University; and Frank Westheimer, Harvard University.