The Advocate, June 7, 1993

EXHIBIT 70A

NHF 443121

Researcher says firms rejected virus preventer

By PETER SHINKLE
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Second in a series

In the early 1980s, drug companies turned down a chemical process that could have prevented the infection of thousands of hemophiliacs with the AIDS virus, according to a leading blood researcher.

The firms could have prevented the AIDS cases by using the process to kill viruses in medicine commonly used by hemophiliacs, said Dr. Edward Shanbrom.

Shanbrom, who designed the process, said he offered it to the companies but they rejected it.

Officials in the blood products industry dispute Shanbrom's claim and question the efficacy of the process he offered.

But some hemophiliacs point to Shanbrom's account as evidence of negligence companies that made the medicine.

Shanbrom was recognized in the 1960s for his leading role in developing the hemophilia medicine, a concentrated blood-clotting protein drawn from blood plasma.

In the early 1980s, the medicine — known as Factor VIII — became contaminated with the AIDS virus, transmitting the disease to as many as 10,000 hemophiliacs.

In 1980, Shanbrom said he began offering the companies a process for killing viruses such as hepatitis in plasma.

By the end of 1982, when the first cases of hemophiliacs with AIDS had become known, Shanbrom had offered the process to four firms that made the medicine, to the American Red Cross and to the New York Blood Center, a large blood bank that supplies New England hospitals, Shanbrom said. They all turned it down, he said.

At the time, the AIDS virus was unknown, but infection with the hepatitis virus was a widespread problem among hemophiliacs.

Shanbrom said he doesn't know why the firms rejected the process, although he suggested that concerns about corporate profits might have obscured the importance of fighting disease. The process would have increased costs, although the increases would not have been great, he said.

"Too often, the executives involved just didn't know. They're too busy balancing the financial sheet," Shanbrom said.

The high rate of turnover among executives also made it difficult for the firms to focus on such issues as fighting viruses, he said.

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Decade-old policy feud persists in AIDS battle

By PETER SHINKLE
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In the early years of the AIDS epidemic, two key federal health agencies clashed over how to respond to the threat AIDS posed to hemophiliacs.

The hard feelings — and the dispute over the proper response to the disease — persist.

The agencies, the Food and Drug Administration and the Centers for Disease Control and Prevention, were on the cutting edge of the government's response to the AIDS epidemic.

Acrimony between the agencies arose in 1982 when CDC officials recommended measures to reduce the risk of infection, while the FDA opposed some of the measures.

By law, the CDC's job was to control AIDS and other diseases, but the agency had no power to order firms to act. The FDA had legal authority to regulate companies that make medicine for hemophiliacs from blood plasma.

Dr. Don Francis, a former CDC hepatitis specialist who later was the chief of CDC's AIDS labs, said the FDA failed to listen to the government's top specialists on the disease — who were at the CDC.

"They really killed a lot of people," he said of FDA officials. "There's a lot of denial. To carry on with their life, they've got to say, 'We did our best.' That's just not true."

Francis said FDA officials "didn't really sit down with the experts at the CDC and listen to the data."

FDA inaction stemmed from the

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"There is arrogance, there is ignorance and there is incompetence, and that may amount to negligence" in the blood products industry, he said.

"But I know that no one ever had evil intent," he said.

Thomas Drees, former president of one of the four companies, Alpha Therapeutic Corp. of Los Angeles, said researchers at his firm told him Shanbrom's process "would not work."

However, Drees acknowledged there might have been a "not-invented-here syndrome," a tendency to reject a process not developed by Alpha, Drees said.

Also, since hepatitis sometimes takes up to 30 years to kill people, and by the mid-70s a test was being used to detect the virus in blood, there was little pressure on the companies to take more steps to address the hepatitis problem, Drees said.

Don Hyman, spokesman for Miles Inc., another Factor VIII maker, said he was unfamiliar with Shanbrom and could not comment because the company's actions have become the subject of court cases.

Hyman said courts have consistently found that "at all times we took every step possible, with all available scientific knowledge, to assure the safety of our clotting products."

Geoffrey Fenton, spokesman for Baxter Health Care Corp., a Factor VIII maker, said Shanbrom offered the process to Baxter in 1980.

"We didn't think it had much merit," Fenton said.

In addition, the firm was in the "advanced development stages" of another anti-viral process, and adopting Shanbrom's process would have taken the firm "back to square one," Fenton said.

In 1983, roughly three years after Shanbrom proposed his process, Baxter began selling Factor VIII treated under the firm's own process, Fenton said.

Shanbrom's account has won support from the Hemophilia/HIV Peer Association, a group that is calling for a congressional investigation of the AIDS epidemic, particularly its impact on hemophiliacs.

Michael Rosenberg, president of the group, said the industry's rejection of Shanbrom's process demonstrates that the industry was not interested in protecting the health of hemophiliacs.

The industry knew before 1970 that Factor VIII posed a threat of hepatitis to hemophiliacs, but it failed to address that threat and failed to warn hemophiliacs about it, he said.

"The safety of hemophiliacs was neglected," said Rosenberg, a hemophiliac who has AIDS.

Photo courtesy of *Allegheny*, the Allegheny College alumni magazine

Dr. Edward Shanbrom said he saw 'ignorance' in the blood products industry, but no evil intent.

The AIDS epidemic among hemophiliacs could have been largely avoided if the manufacturers had simply used the process, which relies on detergents to kill viruses, Shanbrom said.

Supporting Shanbrom's account is the fact that his patented process was purchased in 1988 by the New York Blood Center, which has licensed a similar process to Factor VIII makers around the world.

The Blood Center bought Shanbrom's patents for an undisclosed price in 1988 to make sure there was no cloud over the center's legal claim to its own process, said Dr. Bernard Horowitz, director of the Blood Center's virus inactivation laboratory.

Shanbrom received three patents on his process by 1983, three years after he first requested the patents in 1980. The first AIDS cases in hemophiliacs were reported in July 1982.

Shanbrom's process could have killed the AIDS virus, but at the time it was untested and not supported by data, Horowitz said.

"He didn't have very much data to say, 'Here's a methodology that would work,'" Horowitz said.

In addition, Shanbrom's patents were "just an idea," and hadn't been tried out, Horowitz said.

In fact, Shanbrom said, he had "enormous amounts of data" that he developed while working as a consultant to Armour Pharmaceutical Co., a Factor VIII maker, and other firms.

An Armour spokesman refused to comment.

Shanbrom said although his patent listed a number of detergents, it would have taken a company no more than a year to select a detergent and develop an effective purification system.

During the 1960s, Shanbrom was medical director and director of research at Hyland Laboratories, a division of Baxter. Under his direction, Hyland researchers developed concentrated Factor VIII.

To make the medicine, up to 20,000 donations of blood plasma were pooled, and then the Factor VIII protein was removed from the pool and concentrated.

The medicine revolutionized the treatment of hemophiliacs, who began in the 1970s to live longer and enter the mainstream of American life.

"It was a golden age for hemophiliacs," said Alan Brownstein, executive director of the National Hemophilia Association. From 1972 to 1982, the median age of American hemophiliacs rose from 11 years to more than 20 years, he said.

But the medicine also carried the seed of destruction.

In the early 1980s, the use of large pools meant one plasma donation infected with the AIDS virus could contaminate thousands of Factor VIII doses from the same pool.

"It's sad," Shanbrom said in a pensive moment during a telephone interview from his home in Santa Ana, Calif. "I'm one of the ones who helped spread the disease.

"I will never be able to compensate for the harm done," he said.

He did try to prevent that harm, he said. Shanbrom said he recognized the threat of viruses to hemophiliacs "very early," and immediately began thinking about a solution.

But in 1970, Shanbrom left Hyland, now a division of Baxter Health Care Corp. Shanbrom said he left because he had "strong differences of opinion" with the firm's president over the need for further research on plasma products like Factor VIII. Shanbrom particularly wanted the firm to investigate viruses in its blood products, he said.

Fenton, the Baxter spokesman, said he could not comment on Shanbrom's departure from the firm.

After leaving Hyland in 1970, Shanbrom continued working on the problems of viruses in plasma products, he said. He developed his

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process working as a consultant for medical and pharmaceutical research firms, he said.

The first signs of the virus problem showed up in the spread of hepatitis, a viral infectious disease that can take years to kill a person.

During the 70s, medical journals reported that hepatitis was striking hemophiliacs and workers in plants where plasma was processed into Factor VIII.

In 1976, the U.S. Food and Drug Administration required blood collection centers to test for hepatitis B in donated blood.

But problems with hepatitis continued. In the mid-70s, researchers found that hepatitis viruses other than hepatitis A and B in the blood supply were striking hemophiliacs and others.

By the late 1970s, liver disease from hepatitis was a leading killer of hemophiliacs, second only to the uncontrolled internal bleeding caused by the disorder, Brownstein said.

While, in Europe, a German maker of Factor VIII developed in the late 1970s a process for using heat to kill viruses in plasma.

Neither Shanbrom's detergent process nor the heat treatment process were in regular use in the United States when the AIDS virus entered the blood supply in the early 1980s.

"Hemophiliacs were sitting ducks for any new virus in the blood supply," Rosenberg said.

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Reagan administration's policy of curbing government intervention in the marketplace, Francis said.

FDA spokeswoman Monica Revelle said the two agencies have a "collegial" working relationship, and she declined to respond to Francis' remarks.

FDA officials refused to be interviewed, but Revelle released a statement saying, "FDA did what was scientifically advisable based on the judgments of the world's experts and the state of technology at the time."

One former FDA official, who oversaw blood banks, derided a CDC recommendation as "nonsense."

The dispute flared up in July 1982, when CDC reported three cases of hemophiliacs who had the acquired immune deficiency syndrome, AIDS.

CDC officials warned in a public report that because hemophiliacs commonly injected Factor VIII, a medicine made from blood plasma, it was likely that AIDS was a blood-borne, infectious disease.

But with so few cases of AIDS in hemophiliacs, many in the blood banking industry said they doubted the disease was infectious.

By fall 1982, CDC officials were convinced the disease was caused by a blood-borne virus, said Dr. Bruce Evatt, assistant director of the CDC's Division of Host Factors.

"There wasn't any doubt for us that it was blood-borne in 1982," Evatt said.

However, in its statement to The Advocate, the FDA appeared to discount the significance of the CDC's 1982 findings, saying that "it was not until early 1983 that it was demonstrated that AIDS was infectious."

How AIDS was transmitted "remained a mystery," the FDA said. It was only "by 1984" that scientists established that AIDS could be transmitted by blood, the statement said.

Evatt said the response was similar to the FDA's view in the early 1980s. "At least they're consistent," he said.

After the hemophiliac AIDS cases were discovered, CDC officials began warning that the disease could contaminate the blood supply.

Photo courtesy of Don Francis

Don Francis, former chief of AIDS labs at the Centers for Disease Control and Prevention, said the Food and Drug Administratoln 'killed thousands of people' by its response to the AIDS epidemic.

which posed a particular threat to hemophiliacs, but also to those receiving blood transfusions during surgery.

Factor VIII, the medicine used by many hemophiliacs, is made by pooling up to 20,000 donations of blood plasma. Because of the pooling process, a single blood donation infected with a virus could infect many hemophiliacs.

In January 1983, Francis, Evatt and other CDC officials made recommendations at a meeting at the CDC in Atlanta, which was attended by officials of the FDA, the blood products industry, the American Red Cross and other groups.

Gays and others objected to what they saw as a civil rights violation in a recommendation that people who had had homosexual sex should be barred from donating blood.

Several groups expressed doubt that the disease was infectious, according to accounts of the meeting. Francis pounded his fist on a table in frustration.

Days later, Francis wrote a memo that now seems prophetic:

"I feel there is a strong possibility that some post-transfusion AIDS and much post-Factor VIII receipt AIDS will occur in this country in the coming two years," he wrote.

"For hemophiliacs I fear it might be too late," he wrote.

One key recommendation made at the Atlanta meeting was to test blood for an antibody to hepatitis B to prevent contamination of blood with the human immunodeficiency virus, or HIV, which causes AIDS.

The FDA had required blood banks to use a hepatitis B test since 1976. CDC officials were now recommending the hepatitis antibody test because it was more sensitive than the earlier test and much more likely to disqualify donors who carried the AIDS virus.

CDC officials had found that about 88 percent of the people who had AIDS were found to have the hepatitis B antibody. Therefore, rejecting blood of donors who tested positive for the antibody would significantly reduce the risk of the AIDS virus entering the blood supply, Francis said.

FDA officials rebuffed the idea.

In May 1983, the FDA denied an application by a firm that sought to use the test for the hepatitis antibody. There was an "absence of some data indicating increased safety," the agency told the firm in a

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Dr. Dennis Donohue, director of the FDA's blood and blood products division from 1980 to 1985, said the hepatitis test proposed by Francis and others was "absolute nonsense."

Donohue said the fact that the people with AIDS had had hepatitis B did not prove much. Many of them would also have tested positive for other conditions, he said.

"It's just not scientifically, sufficiently sound that one could apply that to the entire blood supply of this country," Donohue said.

Donohue knew the needs of the blood banks. He established a blood bank in Seattle in 1972 and ran it until he joined the FDA.

Evatt, however, said Donohue's objections were a "smoke screen." Using the hepatitis B test would have prevented infections with both the AIDS and hepatitis viruses, he said. "Donohue is wrong."

Evatt said the test would have forced blood banks to reject about 7 percent of their donors — the source of the blood banks' most important raw material as well as their income.

"The attitude of many blood bankers was that these people would have died anyway if they didn't get a transfusion, so it didn't matter if they got hepatitis," Evatt said.

In fact, the hepatitis B antibody test should have been mandated by the FDA years earlier to prevent hepatitis infection, Evatt said.

At the time no test for the hepatitis B antibody had passed the FDA's rigorous approval regimen, so no test was legally available, Donohue said.

Evatt dismissed that objection, saying that one company had developed a test and it could have been "brought on line very quickly."

The FDA finally recommended the antibody test in 1991 — for use against hepatitis, not AIDS.

In 1984, HIV was discovered, and in 1985, a test to detect the virus was developed and put in use.

Ultimately, by about the beginning of 1987, up to 10,000 hemophiliacs had become infected with HIV, the CDC estimates.

Evatt said it is unclear how many hemophiliac AIDS cases would have been prevented if the FDA in January 1983 had banned the high-risk groups—people who tested positive for the hepatitis antibody, gays and drug-users—from donating blood.

But such a ban would have prevented more than half of the estimated 1,700 AIDS cases caused by blood transfusions from 1983 through 1985, Evatt said.

One industry document suggests Donohue worked with the blood products industry to help it stave off new regulations by the FDA.

The document is an internal memo, dated Dec. 12, 1982, and written by an official of Cutter Biologicals, a division of Miles Inc., one of the major U.S. makers of Factor VIII. The memo was released during a court trial of a lawsuit filed by a hemophiliac against Cutter.

In the memo, Cutter official S.J. Ojala said Donohue requested information about Cutter's plans to address the AIDS threat so Donohue could use the information to stave off efforts to regulate the companies.

Donohue recommended that Cutter consider not using blood collected in prisons to make its Factor VIII products, the memo said.

"Donohue requested that we send him some official notification of our plans so that he could use this as ammunition that voluntary efforts of the industry precluded the need for any further regulation...," the memo said.

Donohue and the FDA refused to comment on the memo.

Hemophilia Medicine and Viruses - A Chronology

1968 — Concentrated Factor VIII, a blood-clotting protein used for treating hemophilia, is put on the market by Baxter Laboratories. Dr. Edward Shanbrom, a Baxter employee, directed the research team that developed the product, which is made by pooling up to 20,000 donations of plasma.

1970 — Shanbrom resigns from Baxter after disagreements with the company over his call for further research on viruses in Factor VIII and other blood products, Shanbrom said.

1970s — Hepatitis strikes hemophiliacs and health industry workers. The disease is the second leading killer of hemophiliacs at the end of the decade, according to the National Hemophilia Foundation.

1980 — Shanbrom begins offering a process for killing viruses in Factor VIII to Baxter, other Factor VIII manufacturers, the Red Cross and others, Shanbrom claims. His process uses detergents to kill viruses. None of the firms adopt his process.

Oct. 6, 1980 — Shanbrom files patent application for his process.

June 5, 1981 — The U.S. Centers for Disease Control (CDC) issues its first public report on the syndrome that is striking gay men, giving them unusual forms of cancer and pneumonia.

July 9, 1982 — The CDC issues a warning that three hemophiliacs have the syndrome marked by a weakened immune system, which is striking homosexuals nationwide. Two of the three hemophiliacs die. The three cases raise the possibility that the illness is transmitted by blood, the CDC says.

July 27, 1982 — The U.S. Department of Health and Human Services calls together an array of health officials and blood industry officials to discuss the three reported cases of the syndrome in hemophiliacs. The disease is given the name Acquired Immune Deficiency Syndrome, AIDS.

Jan. 4, 1983 — At a meeting in Atlanta, CDC officials recommend an array of steps to prevent AIDS transmission, including use of a hepatitis antibody test to screen out blood that is at risk of transmitting the agent that causes AIDS.

May 3, 1983 — The U.S. Food and Drug Administration tells a Factor VIII manufacturer that there is an "absence of some data" to indicate that the hepatitis antibody test would reduce the risk of AIDS transmission from Factor VIII.

April 23, 1984 — U.S. officials announce discovery of the AIDS virus.

March 2, 1985 — U.S. officials announce the licensing of a test for the AIDS virus, and it is soon put into use at blood banks nationwide.

1985 — The New York Blood Center receives a patent for a process using detergent and solvent to kill the AIDS virus in blood. The process is soon licensed to Factor VIII manufacturers.

1987 — Thanks to the AIDS virus test and anti-viral processes, Factor VIII products are considered almost entirely safe from the AIDS virus, according to the National Hemophilia Foundation.

1988 — Dr. Edward Shanbrom sells his patent to the New York Blood Center for an undisclosed amount. The Blood Center buys Shanbrom's patent to avoid any legal questions about the center's right to its process, which it has licensed to Factor VIII makers around the world, Blood Center officials said.

Sept. 10, 1991 — The U.S. Food and Drug Administration recommends that blood banks use the hepatitis B antibody test on blood donations to prevent hepatitis infection, not as a means of preventing AIDS infection.

Sources: documents of the Centers for Disease Control, Food and Drug Administration and U.S. Patent Office; news accounts, interviews.

Advocate graphic by Alice M. Verberne