

www.nytimes.com

**The New York Times**  
ON THE WEB

JUL 17, 2001

## Johns Hopkins Admits Fault in Fatal Experiment

By GINA KOLATA

**B**ALTIMORE, July 16 — Johns Hopkins University said today that it accepted full responsibility for the recent death of a volunteer in an experiment. In a report on its investigation into the death, the university said the researcher who conducted the experiment and the ethics committee that approved it had failed to take adequate precautions to protect research subjects.

"Regardless of the fact that we are unlikely ever to know precisely how or why this happened, Hopkins takes full responsibility for what did happen," said Dr. Edward B. Miller, the dean and chief executive of Johns Hopkins Medicine.

The volunteer, Ellen Roche, died from lung failure on June 2. Ms. Roche, a 24-year-old technician at the university's asthma and allergy center, had been ill since May 5, one day after she inhaled an experimental compound as part of a study to understand the cause of asthma.

Ms. Roche spent several weeks in an intensive care unit. Her air sacs collapsed, her lungs became stiff, air began to leak out of them, her organs began to fail, and, finally, her family decided to remove her life supports.

The fatal illness probably was precipitated, university officials said, when Ms. Roche took a drug in the study. The study was conducted at the center where she worked, but not by the researcher she worked for. She was healthy, and the study was not intended to help her personally. Volunteers were paid up to \$365 for their time and effort.

While stressing that they might never know why Ms. Roche became so ill and died, the medical center's internal committee wrote in its report that they believed the drug she took "was either solely responsible for the subject's illness or played an important contributory role."

The report is being submitted to the federal Office of Human Research Protection.

"This was a horrible tragedy," said Dr. Miller at a solemn news conference today to release the medical center's report. Dr. Miller said another committee, of experts from outside the university, was also investigating and would issue its report by late summer. The Food and Drug Administration and the Department of Health and Human Services are investigating as well.

The New York Times

Enjoy Home Delivery 50% Off!

The New York Times

Best Coverage

News

Culture

Politics

Economy

Business

Plus: Sports, Science, Arts, House & Home and much more.

Click Here

The university has suspended all of the 10 studies being conducted by the principal investigator, Dr. Alkis Togias, an associate professor of clinical immunology.

Joann Rodgers, a university spokeswoman, said the university was "having discussions with the family." But she did not know whether a lawsuit had been filed.

The report issued today depicted a study that went horribly awry. And it raises questions of what is required to assure the utmost safety for volunteers in research. The study was investigating why healthy people and people with asthma responded so differently to substances that constricted their airways. When the constriction occurs, people without asthma can breathe deeply and make their airways relax, but those with asthma cannot get their airways to relax.

The researchers hypothesized that nerves in the lungs controlled this relaxation. They proposed constricting the airways of volunteers with one drug and then giving them a second drug, hexamethonium. That drug temporarily blocks the nerves in their lungs from responding normally. The combination of drugs can simulate an asthma attack.

Hexamethonium, however, is not approved by the Food and Drug Administration. Dr. Togias reported to the institutional review board, or I.R.B., an ethics group overseeing his work, that had concluded that the drug's main risk was in causing a temporary drop in blood pressure. His conclusions were reflected in a consent form signed by Ms. Roche and the other study volunteers.

That form "should not have been approved" by the institutional review board, the Hopkins investigating committee concluded. The form did not mention that hexamethonium was not approved by the F.D.A., and it did not say that the drug's safety was uncertain or that the only data on the safety of inhaling it came from the experience of just 20 people. In addition, the committee found that Dr. Togias had apparently missed some papers suggesting that the drug might injure the lungs.

"The majority of the committee believed that the I.R.B. should have required more evidence of safety in the use of hexamethonium," the report says.

Ms. Roche was the third subject in the study to inhale hexamethonium. The first subject developed a cough and shortness of breath upon exertion. Those effects lasted for a week. But Dr. Togias did not report that subject's symptoms to the review board overseeing the study, reasoning that they were not serious and that they were probably due to a cold that was going around in the research unit, or to the acidity of the hexamethonium solution.

A few days after the first subject recovered, Ms. Roche took the drug, became ill and went to the hospital. Dr. Lewis Becker, the chairman of the internal committee, said he did not blame Dr. Togias for not recognizing the possible significance of the first volunteer's reaction to the drug.

"I can completely understand how he could have attributed it to a cold or the high acidity of the solution," he said. But, the committee said, Dr. Togias should have reported the first subject's experience to the review board.

The committee said the university would redouble its efforts to ensure safety in its clinical research. And that raised questions of whether the Food and Drug Administration should have been involved. The committee said in its report that the institutional review board should have asked Dr. Trogia to find out whether he needed the F.D.A.'s approval to do the study. The agency, Dr. Miller said, often has information from drug company studies that can address safety questions. It could also have required the Hopkins researchers to do additional studies of their own, perhaps giving the drug to animals, before giving it to people.

Drug companies are required to get F.D.A. permission before doing a study like the one at Johns Hopkins, said Dr. Bert Spilker, senior vice president for scientific and regulatory affairs for Pharmaceutical Research and Manufacturers of America. Complying with the agency's requirements typically would take one to two years and cost \$1 million to \$5 million, Dr. Spilker said.

The F.D.A. used to exempt most academic research from this process, said William Vodra, a former F.D.A. lawyer who now works for the law firm Arnold & Porter in Washington. But, he said, with recent problems, including the death of a subject in a gene therapy study at the University of Pennsylvania, that policy "was shaken to the core."

But if the F.D.A. did require universities to adhere to the same standards for research studies as industry, it was not clear where the money would come from, he said.

"I don't think society will be comfortable with industry picking up the tab," Mr. Vodra said. "And I don't think George Bush wants to repeal his tax cut to pay for this."

[Copyright 2001 The New York Times Company](#) | [Privacy Information](#)