

field. Previously secret numbers now available include the approximate temperature of the hohlraum—up to 300 eV, or 3.5 million degrees kelvin—and the approximate size of the hohlraum and pellet—roughly a millimeter and one-third of a millimeter, respectively. But information on underground ICF experiments involving nuclear explosions, as well as computer codes modeling thermonuclear reactions that predict pellet performance, is not expected to be declassified. (The codes could be scaled up to match the parameters for weapons.)

For the moment, however, many practicing researchers in ICF are simply happy to be

free of some of the shackles on normal scientific discourse. Particularly satisfying is a loosening of the “no comment” rule, which prohibits reaction to research presented openly by scientists from other countries if the work would be considered classified by the U.S. government.

Those restrictions have muzzled Melissa Cray, acting head of ICF at Los Alamos National Laboratory, during visits to foreign research institutions. “All I can say is ‘Mm... Mm-hm,’” explains Cray. “Even ooh-ing and ah-ing is not allowed—that counts as a comment. It’s been a pain in the butt.”

Rank-and-file researchers in ICF are still

learning how the guidelines will affect dissemination of their work. Some wonder, for example, if use of classified codes in part of a study will make the entire work ineligible for publication. “I think everyone’s excited about being able to publish,” says Chris Keane, a physicist at Livermore. “But I don’t know if there’s going to be a stampede.” Whether it’s a stampede or just a leisurely walk, however, researchers on ICF are starting to feel much better about the conditions under which they do science.

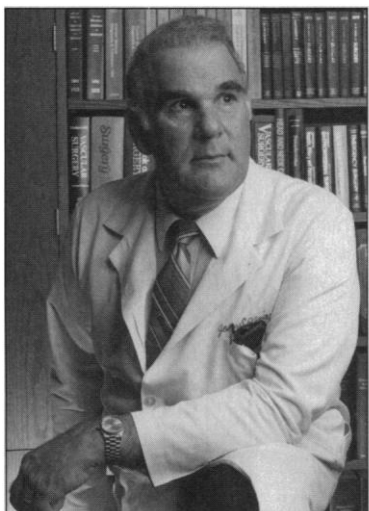
—James Glanz

*James Glanz is a science writer in Chicago.*

## RESEARCH ETHICS

### Scandal Scars Minnesota Medical School

University of Minnesota organ transplant researcher Arthur Matas knew that relations between the medical school and the university administration had finally hit rock bottom when he received an anonymous response to a memo he wrote to the university’s president and board of regents. “If your academic and surgical skills are as inept as your writing ability, it is no surprise that the transplant program has fallen into disrepute,” the venomous missive begins. Matas had complained about the administration’s crackdown on the medical school in the wake of a scandal involving the manufacturing and sale of an experimental drug to prevent the rejection of transplanted organs. But the response made it clear someone in the administration



**Surgical removal.** Transplant surgeon John Najarian is under fire.

saw the medical school faculty as profiteering prima donnas who deserved to be punished. “You ask how things can have deteriorated to this point,” the poison-pen letter continued. “The answer is simple—it’s greed.”

Strong words. But sentiments like these have become the norm at the University of Minnesota, where a scandal in the medical school’s transplant surgery program, one of the top two in the nation, has pitted faculty against administrators and may cost the school some of its leading researchers. Investigations over the past year have revealed that an arm of the medical school’s transplant department manufactured and sold a leading antirejection drug for more than 20 years without necessary federal approval. The resulting fallout has raised questions about the university’s ability to properly oversee researchers who become involved in commer-

cial ventures. And outside the university, patients and transplant surgeons are trying to cope with the loss of what many consider to be the best and least expensive immunosuppressant drug available.

More than a year after the local paper, the *Minneapolis-St. Paul Star Tribune*, first raised questions about the drug sales, separate university and federal investigations have brought many of the facts in the tangled affair to light. In 1971, University of Minnesota transplant surgeon John Najarian received permission from the Food and Drug Administration (FDA) to manufacture and experimentally use a drug, antilymphocyte globulin (ALG), that prevents the immune system from rejecting transplanted organs. Since then, at least 50,000 transplant patients have been treated with ALG, which is available only from the Minnesota program, generating sales exceeding \$60 million.

There’s only one problem: The sales were almost all illegal, since ALG has never been approved for commercial use. Until 1980, interstate sales of investigational new drugs (IND) were prohibited, and after that they were allowed only under certain circumstances with explicit FDA approval. The news shouldn’t have been a surprise to ALG program officials: The FDA told ALG program officials on five occasions over 19 years that they could not sell ALG, according to a university investigative report released in October.

**Who’s to blame?** Last year the ALG program came to a screeching halt when the FDA placed a “clinical hold” on ALG, pro-

hibiting its use. Among the offenses cited were the fact that, although ALG was officially an experimental drug in clinical trials, case reports for many of the estimated 100,000 patients who got the drug were never filed, informed consent was not always obtained, and some side effects and three deaths related to ALG were not reported to the FDA.

The FDA and federal law enforcement agencies began investigations to determine whether criminal charges were warranted and, if so, whether they should apply only to individuals or to the university as a whole. In response, the administration hired two law firms and accused the ALG program of having misled university officials about the legal status of the drug and of failing to notify the university of FDA’s concerns. In September 1992, the university began procedures to fire Richard Condie, the program’s director, and later accused him of diverting \$174,000 from ALG-related revenues to his personal bank accounts. A federal grand jury is investigating Condie in connection with the ALG sales, and earlier this month he resigned from the university. (Condie says the \$174,000 represented legitimate consulting fees.)

The reverberations continued into 1993. In February, university president Nils Hasselmo asked Najarian to resign as head of the surgery department and took away the department’s oversight of the ALG program. By June, both the university’s vice president for health science and the dean of the medical school had resigned. In October, the university began proceedings to strip Najarian of tenure and fire him.

As federal investigators pore over the case, one question stands out: Why didn’t Minnesota simply file the paperwork to make ALG sales legal? Najarian says the program was trying to do just that when the FDA shut it down last year. After clinical trials have shown efficacy, he says, “there is one rule of getting a license, and that is that [the drug] must come from a licensed facility.” Univer-

sities are not licensed facilities, so the program was forced to build a separate ALG factory that could be approved by the FDA. It took several years to save enough ALG income to amass the \$12.5 million required to construct the building, which was finally completed in 1987. But the new facility had technical troubles and has yet to produce any ALG or be FDA certified. Up to now, the drug has been made at a number of university facilities.

But despite the warnings that ALG should not be sold, the program continued to charge for it. For this, Najarian blames inexperience, clouded by good—if misguided—intentions by researchers not overly familiar with regulatory agencies. "You're dealing with a bunch of university professors who do research, not run companies," he says. "ALG was [developed] to save lives. When it became a production facility, it was something we weren't used to doing."

**Cracking down.** For many observers, it is the FDA's behavior that is the real mystery. The FDA refuses to comment on the case, but some observers speculate that, because ALG was the first major drug to be produced and manufactured by a university, the FDA was ill-prepared to oversee such an arrangement. Another explanation for FDA's conduct is that the ALG sales were essentially a victimless crime, since the drug is considered safe and effective and proceeds from its sale were mostly plowed back into the research program. (With the exception of Condie, no one has been accused of personally profiting from ALG.) And some surgeons outside the program have suggested the FDA was goaded into action by pharmaceutical companies that sell competing immunosuppressant drugs.

Whatever the reasons for FDA's delay, when the regulators did crack down, they did so with a vengeance. Beyond the FDA probe, the Federal Bureau of Investigation, the Internal Revenue Service, and the local U.S. Attorney's office have all now mounted investigations. The university, fearful of federal sanctions, responded by taking a hard line with the medical school, including financial audits, management changes, and iron-fisted oversight.

In August, the university's General Counsel abruptly withdrew an application to renew an \$800,000 a year grant from the National Institutes of Health covering 20 faculty researchers (including Najarian) from six departments. University General Counsel Mark Rottenberg said the application, which was for research connected to the ALG program, "contained misleading representations and omissions." Just 1 month later, how-

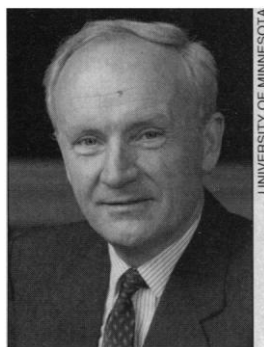
ever, after reviewing the grant with the researchers, university administrators resubmitted the application with only minor changes.

The intervention enraged medical school faculty, who saw it as an infringement of their rights as scientists. "This action, which has prevented faculty from exercising their academic responsibilities for research, is an attack on the academic freedom of the faculty and constitutes a clear violation of due process," wrote a group of 30 senior medical school faculty in a letter to Hasselmo. Rottenberg says the grand jury's investigation of the matter makes the case "highly unusual."

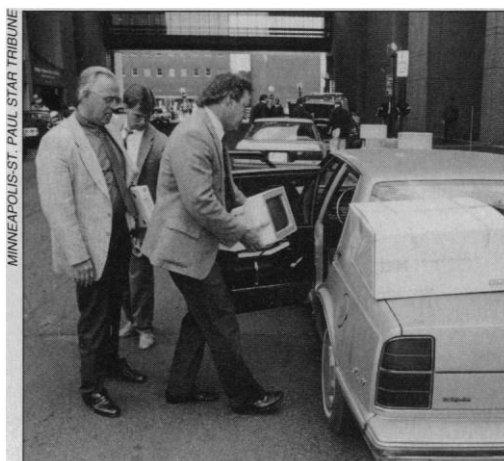
Such episodes had already badly torn the fabric of faculty-administration cooperation.

But whatever comity remained dissolved in October when the administration took steps to oust Najarian, a leading figure at the medical school and, according to the Institute of Scientific Information, the 14th most prolific researcher in the world during the 1980s. Researchers say the administration is looking for a scapegoat for the insufficient oversight of the ALG program. "Our president is trying to save his own fanny and those of the Board of Regents by making John Najarian the fall guy," says Robert Miller, chairman of the physiology department.

**Heavy fallout.** Matas, one of the researchers on the NIH grant, estimates the ongoing battles with university administrators have cost him a year of research. He receives more



**Corrective action.** University president Nils Hasselmo wants changes.



**Hands-on science?** IRS agents load a computer and files from Minnesota's ALG program during an October raid at the hospital.

than \$1 million annually from NIH, and normally publishes from 30 to 40 articles a year. "But now my creativity has gone into arguing with the administration" about what they knew of the ALG program, he says.

The cost to the transplant program appears even higher. At least four top trans-

plant faculty members, including Najarian's heir-apparent, David Sutherland, are considering job offers from other institutions. Arthur Caplan, a bioethicist at the medical school who was not involved in the scandal, says that the clash has led to a "significant increase in vulture behavior" as other institutions capitalize on the medical school's woes by attempting to lure away top faculty. Caplan should know—early next year he'll be leaving to join the faculty of the University of Pennsylvania.

Medical school faculty aren't shy about expressing their dismay. "The morale of the whole medical school is very, very low," says Edward Humphrey, acting head of surgery. Other recent scandals have further disrupted academic harmony. Last month, Barry Garfinkel, a prominent child psychiatrist, was sentenced to 6 months in prison for falsifying data involving research on an antidepressant drug (he is appealing). And the former head of the urology department, Elwin Fraley, resigned in August after a university investigation raised questions about his private use of department funds. As a result of these and the ALG scandal, says Leonard Wilson, head of the history of medicine department, "the whole sense of institutional security has been destroyed."

At the moment, an uneasy truce has broken out at the university. Proceedings to fire Najarian are on hold to allow him time to defend himself in the ongoing criminal investigation of the ALG program. In a 3 November memo to the medical school faculty, Hasselmo concedes that "better oversight might have halted the misconduct sooner" but that "it is also wrong to ignore the fact the [ALG] leadership bears principal responsibility for the serious wrongdoing."

The present investigations are expected to continue for several months, but nobody knows how long the battle will rage between the two warring sides. Last week Winston Wallin, chairman of Medtronic, Inc., of Minneapolis and an unpaid university adviser, told the university's board of regents that "there is almost a complete breakdown of trust" between the Minnesota administration and the faculty of its medical school. As a result, he said, "the quality of the [medical school] is very much at risk."

In the meantime, many see the scandal as regulatory overkill that is depriving patients of an effective drug. The only available alternatives cost at least three times as much and cause more serious side effects, according to Wilson. "One of the tragedies of this whole affair," says Kathleen Terry, a former Minnesota administrator now at the State University of New York, Buffalo, "is that many of the people who need ALG can't get it."

—Christopher Anderson