December 7, 2003

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EDITORIAL

Subverting U.S. Health

In 1955, reporter Edward R. Murrow asked Dr. Jonas Salk who owned the patent on the polio vaccine that Salk had invented. "Well, the people," a puzzled Salk responded. "There is no patent. Could you patent the sun?"

Dr. Salk's professional life was as far removed from that of today's researchers at the National Institutes of Health as the sun is from, say, Wall Street. Theoretically, the NIH belongs to the American people. U.S. taxpayers give it $28 billion a year to develop remedies for human misery. Many assume that today's NIH researchers are carrying on the mission as Salk did, free from financial or commercial pressures that can taint scientific research.

An article on today's front page by The Times' David Willman shows that instead, the NIH has become an arm of commerce, a place where objective science is being trampled in a stampede for market share. Its scientists brazenly collect paychecks and stock options from biomedical companies, and they do so with the blessing of their leaders. With the collusion of those leaders, they are moving swiftly to conceal the sources of their outside incomes from the public.

Who is to know whether a drug is being tested because it really has promise — or because the scientists doing the testing are being paid by the company that developed it?

How can a desperately ill patient in an NIH experiment be confident that the supervisor has only his health in mind, not the earnings of some drug company? Is it credible under such circumstances that the government — that is, the taxpayer — is getting its fair share of the valuable patents that flow from NIH research?

The root of the corruption of the NIH — and "corruption" is the appropriate word — is the Bayh-Dole Act. That 1980 law, ferociously backed by drug makers, let federally funded researchers take out patents and otherwise work closely with "commercial concerns" to profit from their research. The law created technology-transfer offices not only at the NIH but in universities throughout the country whose job was to license their scientists' inventions to whatever company they thought was best able to get them swiftly to the marketplace. It gave agencies such as the NIH the mandate of a for-profit institution, contradicting their original missions. Finally, it gave Harold Varmus, the NIH's director through most of the '90s, the license to demolish private-public firewalls that had served the agency well. In one 1995 memo uncovered by Willman, Varmus ordered all institute and center directors to rescind a policy that had barred them from

accepting consulting fees and stock payments from companies.

The profit motive, revered though it is in America, doesn't always mix well with science. As Mildred Cho, co-director of Stanford's Center for Biomedical Ethics, puts it, "The attitude that financial incentives will help scientists is in direct conflict with the traditional notion that scientists should avoid influences that lead to bias." If there is nothing wrong with such partnerships, as the drug companies argue, then why all the secrecy? NIH employees who make more than $102,168 a year are supposed to publicly report their outside income. Only 6% actually do, because the law is riddled with loopholes and managerial winks. If there is nothing wrong with these lucrative and secret deals, why hide them?

The pharmaceutical industry is everywhere in Washington, all but writing the Medicare prescription drug bill, fielding more lobbyists than there are members of Congress, flinging gifts and trips at doctors and trying to prevent double-blind drug trials that pit one drug against another, instead of against a placebo.

Willman's NIH story, shocking as it is, is just one piece of an unwholesome picture. Congress helped make this system and can help unmake it. Start with high-level hearings. Repeal the most destructive portions of the Bayh-Dole Act. Above all, restore the integrity of the National Institutes of Health.

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Stealth Merger: Drug Companies and Government Medical Research

Some of the National Institutes of Health's top scientists are also collecting paychecks and stock options from biomedical firms. Increasingly, such deals are kept secret.

By David Willman, Times Staff Writer

BETHESDA, Md. — "Subject No. 4" died at 1:44 a.m. on June 14, 1999, in the immense federal research clinic of the National Institutes of Health.

The cause of death was clear: a complication from an experimental treatment for kidney inflammation using a drug made by a German company, Schering AG.

Among the first to be notified was Dr. Stephen I. Katz, the senior NIH official whose institute conducted the study.

Unbeknown to the participants, Katz also was a paid consultant to Schering AG.

Katz and his institute staff could have responded to the death by stopping the study immediately. They also could have moved swiftly to warn doctors outside the NIH who were prescribing the drug for similar disorders. Either step might have threatened the market potential for Schering AG's drug. They did neither.

Questioned later, Katz said that his consulting arrangement with Schering AG did not influence his institute's decisions. His work with the company was approved by NIH leaders.

Such dual roles — federal research leader and drug company consultant — are increasingly common at the NIH, an agency once known for independent scientific inquiry on behalf of a single client: the public.

Two decades ago, the NIH was so distinct from industry that Margaret Heckler, secretary of Health and Human Services in the Reagan administration, could describe it as "an island of objective and pristine research, untainted by the influences of commercialization."

Today, with its senior scientists collecting paychecks and stock options from biomedical companies, the NIH is no longer an island.

Interviews and corporate and federal records obtained by the Los Angeles Times document hundreds of consulting payments to ranking NIH officials, including:

• Katz, director of the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases, who collected between $476,369 and $616,365 in company fees in the last decade, according to his yearly income-disclosure reports. Some of his fees were reported in ranges without citing exact figures. Schering AG paid Katz at least $170,000. Another company paid him more than $140,000 in consulting fees. It won $1.7 million in grants from his institute before going bankrupt last year.

• Dr. John I. Gallin, director of the NIH's Clinical Center, the nation's largest site of medical experiments on humans, who has received between $145,000 and $322,000 in fees and stock proceeds for his consulting from 1997 through last year. In one case, Gallin co-wrote an article highlighting a company's gene-transfer technology, while hiring on as a consultant to a subsidiary of that company.

• Dr. Richard C. Eastman, the NIH's top diabetes researcher in 1997, who wrote to the Food and Drug Administration that year defending a product without disclosing in his letter that he was a paid consultant to the manufacturer. Eastman's letter said the risk of liver failure from the drug was "very minimal." Six months later, a patient, Audrey LaRue Jones, who was taking the drug in an NIH study that Eastman oversaw, suffered sudden liver failure and died. Liver experts found that the drug probably caused the liver failure.

• Dr. Ronald N. Germain, deputy director of a major laboratory at the National Institute of Allergy and Infectious Diseases, who has collected more than $1.4 million in company consulting fees in the last 11 years, plus stock options. One of the companies collaborated with his laboratory on research. The founder of another of the companies worked with Germain on a separate NIH-sponsored project.

• Jeffrey Schlom, director of the National Cancer Institute's Laboratory of Tumor Immunology and Biology, who has taken $331,500 in company fees over 10 years. Schlom helped lead NIH-funded studies exploring wider use for a cancer drug — at the same time that his highest-paying client was seeking to make the drug through genetic engineering.

• Jeffrey M. Trent, who became scientific director of the National Human Genome Research Institute in 1993 and, over the next three years, reported between $50,608 and $163,000 in industry consulting fees. Trent, who accepted nearly half of that income from a company active in genetic research, was not required to file public financial-disclosure statements as of 1997. He left the government last year.

Hidden From View

Increasingly, outside payments to NIH scientists are being hidden from public view. Relying in part on a 1998 legal opinion, NIH officials now allow more than 94% of the

agency's top-paid employees to keep their consulting income confidential.

As a result, the NIH is one of the most secretive agencies in the federal government when it comes to financial disclosures. A survey by The Times of 34 other federal agencies found that all had higher percentages of eligible employees filing reports on outside income. In several agencies, every top-paid official submitted public reports.

The trend toward secrecy among NIH scientists goes beyond their failure to report outside income. Many of them also routinely sign confidentiality agreements with their corporate employers, putting their outside work under tight wraps.

Gallin, Germain, Katz, Schlom and Trent each said that their consulting deals were authorized beforehand by NIH officials and had no adverse effect on their government work. Eastman declined to comment for this article.

Dr. Arnold S. Relman, the former editor of the New England Journal of Medicine, said that private consulting by government scientists posed "legitimate cause for concern."

"If I am a scientist working in an NIH lab and I get a lot of money in consulting fees, then I'm going to want to make sure that the company does very well," Relman said.

Relman and others in the field of medical ethics said company payments raised important questions about public health decisions made throughout the NIH:

• Will judgment calls on the safety of individual patients be affected by commercial interests?

• Can study participants trust that experimental treatments are chosen on merit and not because of officials' personal financial interests?

• Will scientists shade their interpretations of study results to favor their clients?

• Will officials favor their clients over other companies that seek NIH grants or collaborations?

Conflict-of-interest questions also arise in the potentially lucrative awarding of patents.

Thomas J. Kindt, the director of in-house research at the National Institute of Allergy and Infectious Diseases, accepted $63,000 in consulting fees from a New York biotechnology company, Innovir Laboratories, and wound up an inventor on one of its patents.

Asked why the government received no consideration, Kindt said that he had contributed to the "basic idea" while using vacation time.

"No work was done on it as a government employee," said Kindt, whose annual salary at

the NIH is $191,200. His consulting with Innovir was approved by NIH officials, Kindt said.

Others worry that the private arrangements can undermine the public interest.

"The fact that paid consulting is happening I find very disturbing," said Dr. Curt D. Furberg, former head of clinical trials at the National Heart, Lung and Blood Institute. "It should not be done."

Private consulting fees tempt government scientists to pursue less-deserving research and to "put a spin on their interpretation" of study results, he said.

"Science should be for the sake of gaining knowledge and looking for the truth," Furberg said. "There should be no other factors involved that can introduce bias on decision-making."

Dr. Ruth L. Kirschstein, who as the deputy director or the acting director of the NIH since 1993 has approved many of the top officials' consulting arrangements, said she did not believe they had compromised the public interest. "I think NIH scientists, NIH directors and all the staff are highly ethical people with enormous integrity," she said. "And I think we do our business in the most remarkable way."

In response to The Times' findings, Kirschstein said, she would "think about" whether administrators should learn more about a company's ties to the NIH before approving the consulting arrangements.

"Systems can always be tightened up," Kirschstein said on Oct. 29. "And perhaps, based on this, we will do so."

On Nov. 20, NIH Director Elias A. Zerhouni told agency leaders that he would form a committee to help "determine the appropriateness" of employees' consulting and other outside arrangements.

"I believe we can improve our performance by subjecting ethics deliberations to a more transparent process," Zerhouni said in a memo.

In a brief telephone interview last week, Zerhouni said he wanted the NIH "to manage not just the reality, but the perception of conflict of interest."

"If there is something that could be viewed as improper, I think we need to be able to advise our scientists not to get into these relationships," he said. "My sense is our scientists are people of goodwill."

Temptations Abound

The NIH traces its beginnings to the Laboratory of Hygiene, founded in 1887 within a Navy hospital on Staten Island in New York. It became the federal government's first research institution for confronting such epidemic diseases as cholera, diphtheria, tuberculosis and smallpox.

The laboratory's success convinced Congress of its value in seeking cures for diseases.

In 1938, the renamed National Institute of Health moved to its present, 300-acre headquarters in Bethesda, about nine miles north of the White House.

The agency's responsibilities — and prominence — have grown steadily.

In 1948, four institutes were created to support work on cardiac disease, infectious diseases, dental disorders and experimental biology. "Institute" in the agency's name became "Institutes."

President Nixon turned to the NIH in 1971 to lead a war on cancer. The agency has led the government's fight against AIDS. Two years ago, President Bush enlisted the NIH to help counter biological terrorism.

Republican and Democratic administrations have boosted spending for the 27 research centers and institutes that compose today's NIH. Since 1990, the annual budget has nearly quadrupled, to $27.9 billion this fiscal year.

Senior NIH scientists are among the highest-paid employees in the federal government.

With billions of dollars in product sales potentially at stake for industry, and untold fortunes riding on biomedical stock prices, commercial temptations abound:

Researchers poised to make a breakthrough in their NIH labs can, the same day, land paid consulting positions with companies eager to exploit their insights and cachet. Many companies cite their connections to NIH scientists on Web sites and in news releases, despite an agency rule against the practice. Selection of a company's products for an NIH study can provide a bankable endorsement — attracting investors and boosting stock value. If the study yields positive results, the benefits can be even greater.

Conflicts of interest among university medical researchers have received wide attention in recent years. U.S. Rep. W.J. "Billy" Tauzin (R-La.) also raised questions recently about cash awards that several nonprofit institutions made to a previous director of the National Cancer Institute.

The consulting deals between drug companies and full-time, career employees at the NIH, however, have gone all but unnoticed.

The wide embrace of private consulting within the NIH can be traced in part to calls from

Congress for quicker "translation" of basic federal research into improved treatments for patients.

And for decades industry has pressed for more access to the government's scientific discoveries.

As the number of government-held patents soared, companies sought legislation encouraging commercialization of federally funded inventions. The proponents said the changes also would make U.S. firms more competitive with foreign companies whose research and development programs were subsidized by their governments.

Laws enacted in the 1980s for the first time authorized formal research collaborations between companies and scientific arms of the government, including the NIH. Starting in late 1986, in-house researchers at the NIH were permitted to arrange cooperative research agreements with companies. The agreements were intended to benefit both sides while advancing scientific discovery.

Other changes in law permitted the government agencies, and the researchers, to share in future patent royalties for inventions.

The new laws said nothing about government employees being hired by the companies.

Yet by the end of the 1980s, more companies were putting NIH researchers on their payrolls, albeit within limits imposed by the NIH.

Agency leaders in the 1990s began weakening those restrictions.

In November 1995, then-NIH Director Harold E. Varmus wrote to all institute and center directors, rescinding "immediately" a policy that had barred them from accepting consulting fees and payments of stock from companies.

The changes, he wrote, would bring the NIH ethics rules more in line with new, less stringent, executive branch standards. Loosening of restrictions on employees' outside pursuits was occurring throughout the government. And with biomedical companies ready to hire, few were better positioned to benefit than employees at the NIH.

Varmus' memo — which until now has not been made public — scuttled other restraints affecting all employees, including a $25,000 annual limit on outside income, a prohibition on accepting company stock as payment and a limit of 500 hours a year on outside activities.

His memo also offered a narrowed definition of conflict of interest:

Employees had been barred from consulting for any company that collaborated with their NIH lab or branch. But Varmus said the ban would be applied only if the researcher was

personally involved in the company's collaboration with the agency.

Furberg, the former NIH official, said Varmus' actions invited, at minimum, appearances of conflict of interest.

"I'm amazed at what he did," said Furberg, a professor at Wake Forest University. "And to do it in secrecy I find very objectionable. This is a critical change in the NIH policy."

In 1999, Varmus wrote a letter to the institute directors that cautioned them to "avoid even the appearance of a conflict of interest." But in an attachment to the letter, he told them that employees "may briefly discuss or mention current work" to outsiders, in effect giving agency scientists permission to reveal their unpublished, confidential research.

Varmus, now president and chief executive of the Memorial Sloan-Kettering Cancer Center in New York, declined to be interviewed for this article. His spokeswoman, R. Anne Thomas, said that Varmus, who in 1989 shared a Nobel Prize for research into the genetic basis of cancer, believed that NIH employees should take personal responsibility for avoiding conflicts of interest, regardless of what agency rules allow.

Kirschstein, after taking over as Varmus' interim successor at the NIH three years ago, said in a May 2000 speech to medical researchers that conflicts of interest posed "a major concern."

"While the federal government was once the dominant force for supporting clinical research, today we share the arena with biotechnology companies, pharmaceutical firms and many others — all interested in the possibility of financial gain from their research.

"Profit raises issues of public trust," she said. "When scientific inquiry generates findings that can make a profit for the researcher and the institution, their images become clouded."

Yet officials have lifted controls on consulting even as industry's stake in NIH research has deepened. When Zerhouni, the current NIH director, appeared before the House Subcommittee on Environment, Technology and Standards last year, he cited 274 ongoing research and development agreements between the federal agency and industry.

At the same time, NIH leaders have moved to what they describe as "managing" conflicts of interest. Employees are allowed to consult if they receive prior clearance from an administrator at their institute or, in the case of most institute directors, from NIH headquarters.

An Honor System

Potential conflicts are typically addressed by allowing employees to sign "recusals." Under these agreements, NIH employees pledge not to participate in decisions affecting

an outside client. Agency officials, Kirschstein said, rely on an honor system to enforce recusals and other conflict-of-interest rules.

The Times found instances in which the recusals did not work as intended.

In the mid-to-late 1990s, Eastman, the diabetes researcher, participated in a series of decisions affecting the drug company employing him as a consultant, despite having signed a recusal. Separately, Katz, the director of the arthritis institute, signed a recusal involving his client, Schering AG, which nevertheless supplied the NIH with the drug involved in the kidney patient's death in 1999.

Katz said that he did not know at the time that Schering AG was the maker of the drug his institute was testing.

Compliance with the recusals can, itself, undercut the interests of the NIH and taxpayers, who support the agency. When heads of institutes and laboratories recuse themselves, they sometimes constrain their ability to carry out their government duties.

Kirschstein, who for the last eight years has personally reviewed requests from the institute directors to consult privately for pay, said she tended to approve the deals, unless she saw "real conflict."

"I've disapproved some — and I've approved many," she said.

In her view, recusals have worked "extremely well" in avoiding conflicts of interest.

Other present and former officials say it is difficult, if not impossible, for researchers to keep separate their confidential government information when they consult for companies.

"You can't police the thing," Philip S. Chen Jr., a senior advisor in the NIH director's office who has served as an agency scientist or administrator since the 1950s, said in an interview last year. "The rules are there — whether they follow the rules is another thing."

A former NIH director voiced surprise at the agency's loosened approach to conflicts of interest.

"There has been a lot of relaxation," said Dr. Bernadine P. Healy, who served as director from 1991 to 1993. Before, Healy said in an interview, "there were very strict ethics rules for NIH scientists. You couldn't have virtually any connection with a company if your institute was in any way doing research involving their products."

At least one vestige of the old days remains.

During last year's holiday season, workers were advised to refuse gifts from outsiders

worth more than $20.

"Just a reminder," ethics coordinator John C. Condray wrote, introducing a five-page memo, "that sometimes gifts and events can create the appearance of a lack of impartiality."

Fewer Public Filings

While making it easier for scientists to cut consulting deals, the NIH has made it harder for the public to find out about them.

The Ethics in Government Act requires yearly financial-disclosure reports from senior federal employees. This year, employees paid $102,168 or more generally must disclose outside income by filing a "278" form, which is available for public review. Other employees may file a "450" form — which does not specify the amount of money received from an outside party and is kept confidential.

At the NIH, 2,259 employees make more than $102,168, according to data provided by the NIH. Those records show that 127 of the employees — about 6% — are filing disclosure forms available to the public.

From 1997 through 2002, the number of NIH employees filing public reports of their outside income dropped by about 64%, according to the agency records. Most of those employees have switched to filing the confidential 450 form.

At the National Institute of Allergy and Infectious Diseases — which researches treatments for AIDS and other life-threatening maladies — only three officials file public reports revealing their outside income, according to NIH records.

Officials at the NIH said that an advisory legal opinion from the U.S. Office of Government Ethics gave them the discretion to bypass public disclosure.

Issued in 1998, the opinion said that the threshold for public disclosure was to be set, not by a federal employee's actual salary, but by the low end of his or her pay grade. If the minimum salary in an employee's grade is beneath the $102,168 threshold, he or she is exempt from filing a public report.

The NIH has shifted many of its high-salaried employees into pay plans with minimums that dip below the threshold.

For instance, two prominent NIH laboratory leaders, Schlom and Germain, make $180,400 and $179,900, respectively. Within roughly the last year, NIH changed each of their pay plans, and they now are exempt from public disclosure.

They file confidential forms, which instruct employees to not specify the dollar amounts

they receive from outside parties.

Asked why the NIH has assigned highly paid staff to plans that eliminate public disclosure of employees' outside income, an NIH spokesman, John Burklow, provided a written response:

"The primary benefit of the alternate pay plans is to attract and retain the best scientists in a highly competitive environment."

Said Donald Ralbovsky, another NIH spokesman: "What it really boils down [to] is that fewer people are filing 278s because of changes in pay plans."

The shift imparts an implicit message to employees, said George J. Galasso, a former NIH researcher and administrator who retired in 1996:

"If you've got something to hide, you file a 450. If you don't, you file a 278."

Make-or-Break Grants

As director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Katz is one of the few at the NIH who still must file public financial-disclosure reports.

Katz, 62, is paid $200,000 a year — more than members of Congress, justices on the Supreme Court and the vice president.

His institute leads the government's research into the causes, treatment and prevention of disorders of the joints, bones and overall muscle-skeletal system.

With a yearly institute budget of $485.4 million, Katz's decisions are watched closely by industry. The director's office decides how much of the budget will be spent on grants and contracts coveted by companies.

And Katz has been available for outside consultation: From 1993 through 2002, Katz took between $476,369 and $616,365 in fees from seven biotech and pharmaceutical companies, according to his annual disclosure statements. He consulted while chief of the dermatology branch at the National Cancer Institute and continued after becoming arthritis institute director in 1995.

Katz said that his private consulting broke no rules and that he relied in part on Varmus' 1995 memo while entering arrangements with companies.

"The consultations provided my global knowledge as a dermatologist and research scientist," Katz said in written responses to questions from The Times. "I have always received official permission to perform these consultations and have performed these consultations outside of my normal NIH work schedule and according to strict

government guidelines and rules."

One of his clients was Advanced Tissue Sciences Inc.

The struggling biotech company in San Diego hired Katz as a consultant in 1997, a year after he had announced a new NIH research initiative for bone and connective-tissue repair.

Advanced Tissue installed Katz on its scientific advisory board and paid him fees between $142,500 and $212,500 from 1997 through 2002, according to his income-disclosure reports.

During that time, Katz's institute pledged $1.7 million in small-business research grants to the company. The company announced nearly every grant in a news release; Advanced Tissue's president termed the grants "an endorsement by the government."

In his written response, Katz said that he had signed a recusal "withdrawing myself from any interactions between Advanced Tissue Sciences and the government to remove any real or potential conflict of interest." The grants were awarded following evaluations by NIH reviewers outside of Katz's institute.

Responsibility for administering the grants to Advanced Tissue was delegated to one of his subordinates, Katz said.

The NIH policy manual says officials may not take fees from companies seeking or receiving agency grants "if the employee is working on or involved in these matters" or "supervising others who work on these matters."

Katz said his subordinate "handled all decisions regarding these grants without informing me."

However, Advanced Tissue kept him apprised as NIH grants were obtained, a company executive said.

"He was informed," said Anthony J. Ratcliffe, the firm's vice president for research until its collapse a year ago. "We would have made a written report to the SAB [scientific advisory board] members twice a year. There would have been a report to the SAB meetings on all grants, all grant activities."

Ratcliffe said the company dealt with Katz's potential conflict of interest by paying him in fees alone, and not stock options. Both men said Katz did not advise the company on the NIH grants.

His consultations, Katz said, were limited to his scientific expertise and "never involved, directly or indirectly, the preparation or discussion of material which could relate to any

financial dealings between [Advanced Tissue] and the NIH."

Kirschstein, the senior NIH official who each year approved Katz's consulting with Advanced Tissue, said she did not learn the company held grants with the arthritis institute until The Times inquired.

"I didn't even know there were grants," Kirschstein said.

As it turned out, the grants would be among the few positive financial developments for Advanced Tissue.

By December 2001, its cumulative net operating losses were approximately $292.7 million. Barely a year later, the company entered bankruptcy and shut its doors, having collected about $1.5 million of the $1.7 million in small-business research grants.

Life-and-Death Decisions

While Katz was consulting for Advanced Tissue, he also was on the payroll of Schering AG, which made Fludara, a drug that his research staff was using as an experimental treatment for autoimmune diseases.

From the time he began consulting for Schering AG in 1996 through 2002, Katz collected between $170,000 and $240,000 in fees from the company, his disclosure reports show.

In his responses to questions, Katz said that he "first became aware" that Fludara was a Schering AG product when The Times made inquiries.

Fludara had been approved by the Food and Drug Administration in 1991 to treat leukemia, but the company wanted to expand its use to other diseases, a goal the NIH studies could advance.

Two people died in the studies conducted by Katz's institute.

In one study using Fludara to treat muscular disorders, a patient suffered what agency researchers reported in July 1998 as a "sudden death ... not thought to be drug related."

The second fatality, indisputably, resulted from the treatment. It involved "Subject No. 4," who had enrolled in a separate study, designed to treat kidney inflammation related to lupus, a disease of the immune system.

Schering AG provided Katz's institute with a supply of Fludara and with analyses of patients' blood samples through its U.S. affiliate, Berlex Laboratories, records and interviews show. The company also contributed a total of $60,000 to the institute to support the research, eliciting a July 1, 1998, thank-you letter from Katz.

Participants entering the study were warned of some risks. The NIH advised them that Fludara might cause damage to their blood cells and that, as a result, "blood transfusions may be required."

That is what befell Jamie Ann Jackson, identified in NIH documents as "Subject No. 4."

Jackson, a registered nurse, lived with her husband, their two daughters and a son in Plainville, Mass., about 37 miles southwest of Boston. She received four transfusions between March and May of 1999, yet grew sicker.

On June 1, trembling with chills, Jackson was admitted to the NIH Clinical Center in Bethesda. Within days, lab results confirmed that she was in the grip of graft-versus-host disease. The graft of outside material — in this instance, blood from a transfusion — attacks and overwhelms the immune system and organs of the new host.

Fatal in about 90% of cases, the malady had been documented in leukemia and other cancer patients who took Fludara. For that reason, the risk of graft-versus-host disease was noted in the product labeling — as was a warning about irradiating transfusions as a prevention.

But the NIH doctors did not specify that transfusions should be irradiated for patients in the lupus study. In an interview, Dr. John H. Klippel, then the institute's clinical director, said he could not recall whether he or his colleagues took stock of the label warning.

In Britain, authorities were more cautious, recommending that blood transfusions for all patients taking Fludara be irradiated. The British recommendations were described in 1996 in The Lancet, a medical journal with an international circulation.

Two weeks after being admitted to the NIH Clinical Center, 42-year-old Jamie Ann Jackson died.

"Steve Katz was notified almost immediately," Klippel said.

Katz's subordinates warned the remaining patients and their personal doctors about the death and, for the first time, advised them to irradiate any transfusions. The FDA was informed.

But the NIH office responsible for conducting an inquiry into research deaths was not promptly notified.

And while Katz's institute stopped enrolling recruits, the treatment of those already in the study continued for nine months after Jackson's death.

After five of the other 12 patients given Fludara experienced abnormal changes in their blood, increasing their risk of infection, the experiment was stopped, 20 months before its

scheduled conclusion.

'Absolutely No Role'

While Fludara's use for anything other than leukemia remained experimental, an increasing number of doctors were prescribing it "off-label" for diseases of the immune system, including rheumatoid arthritis.

Yet the NIH was slow in warning them about the lethal, but preventable, problem of graft-versus-host disease.

It was not until October 2000, 16 months after Jackson died, that doctors from the NIH briefly summarized the death in Transfusion, the journal of the American Assn. of Blood Banks.

Meanwhile, three articles written by NIH doctors and published from March 2000 through May 2001 referred to the agency's work with Fludara without mentioning the risk of graft-versus-host disease or the death in their study.

In an article published in the May 2001 issue of the journal Pharmacotherapy, the doctors, three from Katz's institute, wrote that Fludara "was well tolerated" and thanked the company for providing the drug and "analytical support."

Not until last week — 4 1/2 years after the event — did the same doctors appear as authors of a full-length article describing Jackson's death. It was published in Transfusion.

In his responses to The Times, Katz said that, to his knowledge, "all matters concerning the adverse event were handled according to standard operating procedures."

Katz said that he had signed a recusal, pledging not to participate in matters involving Schering AG. He said he had nothing to do with initiating the study, "was not advised that it was ongoing and had absolutely no role in overseeing its conduct."

The Times documented three instances in which he discussed the study: The July 1998 letter acknowledging the company's first half of the $60,000 donation; the June 1999 phone call from Klippel notifying him of the death; and a meeting in April 2000 with Kirschstein to discuss the fatality and his institute's response to it.

Katz confirmed all three incidents in a series of e-mail exchanges.

He said he wrote the letter without realizing that Berlex Laboratories was the American arm of Schering AG.

"At that time, I was unaware of any relationship between Berlex Laboratories and

Schering AG and was, therefore, unaware that my sending the thank you letter might present any conflict of interest."

Katz declined to identify when he learned that Berlex was the U.S. affiliate of Schering AG.

The relationship between Schering AG and Berlex has not been a secret. News articles describe Berlex as Schering AG's U.S. business unit. The Berlex and Schering AG Web sites make clear the affiliation. In 1998 — two years after Katz was hired — Berlex accounted for 17% of Schering AG's net global sales.

Oliver Renner, a spokesman in Berlin for Schering AG, said: "Berlex Laboratories is a fully owned subsidiary of Schering AG. We are distributing our products under the name of Berlex in the United States. We also conduct research and development work through our Berlex entities."

Katz, asked about the phone call he received when Jackson died, said he did not then realize what company made the study drug. Although the study was ongoing, he said he did nothing in response to being notified of the death.

"No further action was required or undertaken by me," Katz said.

He said he remained uninformed about Schering AG's connection to the study when he met with Kirschstein in April 2000.

"The reason that I did not exclude myself from any contact regarding the lupus [clinical] trial was that I was unaware, and no one on the staff brought to my attention, that the trial had any relationship to Schering AG," Katz said. He noted that the arthritis institute first used Fludara for lupus in 1993, before he arrived as director.

Representatives of Schering AG said the company did nothing out of the ordinary in collaborating with the NIH — and in hiring Katz.

"The discovery and development of new pharmaceuticals often involves a combination of government and private industry efforts," the company said in a statement. "It is also a common practice for pharmaceutical companies to work with many leading external experts.... In keeping with this practice, we have a consulting agreement with a Dr. Stephen Katz from the NIH involving his expertise in the field of dermatology."

Schering AG is no longer pursuing development of Fludara as a treatment for autoimmune diseases.

Kirschstein, the NIH official who approved Katz's consulting for Schering AG, said she had not known its drug was being tested by his institute.

Kirschstein said she did recall being visited by Katz and his top aide in April 2000. The NIH's human protection office had just opened an internal review of the lupus-related study, questioning the researchers' failure to protect against graft-versus-host disease, as well as their failure to report the death to agency investigators in a timely fashion.

"Dr. Katz and his scientific director came to me ... to tell me about a study in which a drug was used and there was a death," Kirschstein said. "They did not tell me the name of the drug, and did not tell me much about the study, but told me that they and the [department] were looking into it."

In a follow-up letter two years later, the internal review absolved the institute of responsibility for Jackson's death. Her husband has filed a wrongful-death lawsuit against the government in U.S. District Court. The lawsuit does not refer to Katz.

Jackson's mother, Carmella Tarte, said time had not eased her grief.

"We all went to the hospital, but we never even got to talk to her," Tarte said in an interview. "It's been four years and, well, Thanksgiving was just another day, you know? She has children she didn't see graduate."

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E-mail story

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CASE STUDY | RONALD N. GERMAIN

A Federal Lab Leader Who Made $1.4 Million on the Side

David Willman

BETHESDA, Md. — Dr. Ronald N. Germain has been a paid advisor to a dozen drug-development companies, a law firm that specializes in patent litigation and an investment fund that buys and sells biotechnology stocks.

By his own accounting, he has collected more than $1.4 million in fees over the last 11 years and gathered company stock options valued at $865,000.

Germain's full-time job is deputy director of the National Institutes of Health's Laboratory of Immunology, which explores how the immune system protects against infections, cancer and other maladies.

His annual government salary is $179,900 — but his consulting income surpassed it in one recent year and nearly matched it another year.

He has taken fees from a company collaborating formally on research with his laboratory. Another company's founder collaborated with Germain in his NIH capacity. Four more of his clients had grants or research agreements with the institute that houses his lab. He made plans last spring to begin consulting with a new client, a venture capital firm that invests in nascent biotechnology companies.

In written responses to questions from the Los Angeles Times, Germain, 55, said he had always followed NIH rules and had consulted with the approval of agency officials. He said he had not made government decisions affecting companies that paid him.

"I have a well-regarded reputation both inside and outside of NIH for adhering strictly to the rule preventing me from revealing or using specific knowledge of my NIH research during consulting activities and for keeping all outside activities from having any bearing on the conduct of my activities as a [government] employee," Germain said.

By consulting for the companies, he said, "my general insight into immunology and related biomedical sciences can be used to help develop new drugs and treatments for Americans." He said he provided the law firm with "expert opinion on immunological matters." His advice to the investment fund, Germain said, concerned "whether or not I believe that a particular technology or approach has a strong scientific base."

His consulting work also provides his family with "greater financial security," he said. "This is of special importance to me because as a former Hodgkin's lymphoma patient, it was difficult until recently to obtain adequate life insurance coverage while being at increased risk for an early death."

Germain, a graduate of Harvard Medical School, has been deputy director of his laboratory, housed in the National Institute of Allergy and Infectious Diseases, since 1987.

He was warned about conflicts of interest two years ago by an NIH lawyer, Karen Santoro.

But the lawyer's concern focused only on Germain's investments in mutual funds composed of biotech and health-care companies, some of which held contracts with his NIH lab. "Each underlying company may pose a potential conflict," Santoro told Germain in a May 11, 2001 e-mail.

Two companies on the mutual fund list were consulting clients for Germain. Yet Santoro's e-mail said nothing about the fees and stock options they and other companies were paying him.

Germain, in an e-mail to Santoro three days later, agreed to exchange his securities for "holdings that are not concentrated in the health and biotech areas."

Germain told The Times, "Ms. Santoro was fully aware of all my consulting arrangements and compensation."

Many firms for which Germain has consulted have sought to develop products in the same frontiers he or others at the NIH explore, including:

- Genetics Institute, a Massachusetts-based branch of an industry titan, Wyeth.

In 2001, Genetics Institute and Germain's lab entered a formal collaboration called a cooperative research and development agreement, or CRADA, to study the effect that genes have on the immune system. That same year, Genetics Institute paid Germain $37,500 in fees. Germain accepted $25,000 last year.

From 1992 through 2002, the company paid him a total of $322,749, according to Germain's annual income-disclosure reports.

Officials at the NIH have continued to approve Germain's consulting with Genetics Institute despite a provision in the agency's policy manual forbidding employees from taking fees paid by a company that is collaborating with their labs. While the policy remains on the books, a 1995 memo from the NIH director said it would be enforced only if the researcher was directly involved in the collaboration.

Germain said that he was not informed in advance that Genetics Institute and his NIH lab had taken steps to formally collaborate. When he did learn this, Germain said, he approached his institute's ethics office.

"The decision was that my consulting arrangement, having predated the [collaborative agreement], did not need to be terminated," Germain said.

• Mojave Therapeutics Inc., a biotech company developing treatments for cancer and viral diseases.

From 1998 through 2002, the New York firm paid Germain $93,929, plus stock and stock options worth up to $15,000. Germain has been a member of Mojave's scientific advisory board.

Mojave calls itself a leader in developing "heat-shock" proteins as potential therapeutic agents.

While consulting for Mojave, Germain, in his capacity as an NIH scientist, co-wrote a June 2000 journal article describing the role of heat-shock proteins. His co-authors included two scientists affiliated with Mojave, which posted the study on the company Web site.

Germain said he did not consider the study a collaboration with Mojave researchers and did not know the article appeared on the Web site.

The 2000 article, he said, reflected work done in his NIH lab in "an academic collaboration" with researchers at the Memorial Sloan-Kettering Cancer Center. Germain said the project "did not involve Mojave."

However, one of his co-authors, James E. Rothman, was a founder of Mojave and served, with Germain, on its scientific advisory board. Rothman also is an executive at Sloan-Kettering. The other co-author accepted a position at Mojave during the study.

Asked about these circumstances, Germain said that he had known about his collaborators' ties to Mojave, but he considered the work to be only with Sloan-Kettering.

Germain said he had told Rothman "that I would continue the research with Sloan-Kettering only if it were kept separate from the activities of the company," adding:

"I was not a party to the company's posting of this published paper on their Web site and was in fact unaware of this.... Given that Dr. Rothman is an author on the paper, I had no right to demand that the company not display the work on its Web site after it was published."

Rothman declined through an aide to be interviewed.

Germain said that while the research was being done, "I informed my immediate supervisor at NIH of the situation." He noted that his lab's work with heat-shock proteins predated the collaboration.

• Alexion Pharmaceuticals Inc., a Connecticut company developing antibody-based drugs for cardiovascular and autoimmune disorders and cancer.

Alexion collaborated with Germain's lab from 1993 to 1997 under a CRADA.

In 1994, Alexion announced the NIH had signed an agreement giving the company "worldwide exclusive rights to U.S. and foreign patent filings" for discoveries that might result from the collaboration. When the company reported financial results in 1996, it said the NIH collaboration and funding had helped to reduce losses.

Germain became a paid consultant to Alexion in 1998, about a year after his lab finished collaborating with the company. Over the next five years, he accepted $51,000 in fees, plus vested stock options worth up to $100,000.

Germain joined Alexion's scientific advisory board, he said, at the behest of an executive who used to work at the NIH with him.

"He was interested in my acting as a consultant for a long time, both preceding and during the period of the CRADA," Germain said. "I agreed to take the position only after the CRADA ended."

Alexion's head of research, Stephen P. Squinto, said the company relied on Germain and the other scientific board members to review its programs "and potentially introduce us to some newer things, newer technologies or drug targets."

• Cell Genesys Inc., a developer of therapeutic cancer vaccines and gene therapies for AIDS and other life-threatening illnesses.

The company has had a long affiliation with Germain and the National Institute of Allergy and Infectious Disease, which houses his lab.

In financial reports, the company has cited its reliance on a "collaborative relationship" with the institute and its affiliation with Germain, who sits on its scientific advisory board.

The South San Francisco company from 1992 through 2002 paid Germain $352,000 and provided stock options that he has listed as worth up to $250,000. During this period, Cell Genesys collaborated on research with the institute, although not directly with Germain's lab.

Germain said he has "reviewed and provided advice" regarding Cell Genesys' overall research programs.

• MedImmune Corp., a Maryland biotech company that makes treatments for viral diseases and other maladies. MedImmune over the last 11 years has paid Germain $163,350 in fees — plus up to $500,000 in vested stock options.

MedImmune's top-selling product, an antibody for preventing a respiratory infection in infants, was developed jointly throughout the 1990s with the allergy and infectious disease institute. Germain's lab was not involved.

• Hybridon Inc., a Massachusetts pharmaceutical company that develops medicines and diagnostics based on synthetic DNA.

In October 2001, Hybridon's chairman, Dr. James B. Wyngaarden, a former NIH director, announced the hiring of Germain, saying his "expertise and experience in the area of immunology will be extremely helpful."

Hybridon paid Germain $30,000 last year.

In October 2002, Hybridon said it and the NIH had clashed over three agency-held patents, triggered by Hybridon's application for its own patent. The matter, related to synthetic DNA, is pending before the U.S. Patent and Trademark Office.

Both Germain and the chief executive of Hybridon, Stephen E. Seiler, said that Germain's consulting had not involved the patents.

"The only point of contact between us and the NIH is we share Ron's time," Seiler said.

As of last month, Germain no longer must publicly disclose his outside income. He instead will file reports that are kept confidential. Germain said he did not request the change, which was made by the NIH.

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CASE STUDY | RICHARD C. EASTMAN

A Federal Researcher Who Defended a Client's Lethal Drug

David Willman

BETHESDA, Md. — When Dr. Richard C. Eastman talked about the controversial diabetes drug Rezulin, doctors listened. After all, he was the top diabetes researcher at the National Institutes of Health.

Eastman's views were heard clearly in the fall of 1997, when the Food and Drug Administration received reports of liver injury among patients taking the pill.

At the time, Eastman was supervising a $150-million NIH study exploring whether Rezulin or another drug could prevent diabetes in adults who had slightly elevated blood-sugar levels.

In light of the reports of liver injury, an FDA medical officer questioned the prudence of the NIH's nationwide study. Eastman, one of four members of the study's executive committee, said all was well.

"At this point in time, we consider the risk of [Rezulin] to be very minimal," Eastman told the FDA in a Nov. 6, 1997, letter obtained by the Los Angeles Times. "[W]e continue to think that the drug is safe," he wrote. "The risk to benefit ratio in the trial continues to be one that we think is very acceptable."

Eastman signed the letter to the FDA using his government title, director of the NIH's diabetes division. The letter did not disclose that he was also a paid consultant to Warner-Lambert Co., the maker of Rezulin.

The FDA allowed the use of Rezulin to continue in the study. Warner-Lambert went on to collect $2.1 billion in sales revenue from Rezulin before it was pulled from the U.S. market in 2000 after being cited as a suspect in 556 deaths, including 68 that involved liver failure.

Some aspects of Eastman's dual role were reported earlier by The Times. Hundreds of pages of newly obtained internal company and federal documents show that Eastman took previously unreported actions regarding the drug.

Reached by telephone last month, Eastman, 57, declined to be interviewed for this article.

He was hired by Warner-Lambert in October 1995, less than three weeks after he met with a company executive on behalf of the NIH to discuss the drug's safety, records show. As part of his consulting arrangement, Eastman spoke to diabetes "thought leaders" assembled by the company. He also signed a contract prohibiting him from disclosing "confidential and proprietary information" without the company's prior, written consent.

Eastman's consulting was approved in November 1995 by two senior officials, including the then-director of the NIH diabetes institute.

In March 1996, Eastman signed a federal recusal, pledging to disqualify himself "to judge or otherwise act [as a federal official] on any matter or matters pertaining to" Rezulin's status in the NIH study.

However, the NIH has no procedure for verifying that officials comply with the terms of their own recusals. And Eastman continued to participate in decisions of the study's four-person executive committee regarding Rezulin, according to records and interviews.

When the inspector general of the Department of Health and Human Services inquired years later, Eastman said he had not thought he was violating his recusal, records show.

Eastman and his boss also told the inspector general that they had never seen a 1996 memo from an NIH attorney warning Eastman: "recuse yourself from all official matters" involving Warner-Lambert. Both Eastman and his boss, then the deputy director of the diabetes institute, stated that an office aide had filed away the attorney's warning before they had a chance to read it.

From 1995 through 1997, while collecting upwards of $43,000 in consulting fees and related compensation from Warner-Lambert and its affiliates, Eastman repeatedly defended Rezulin in his government capacity.

On Nov. 28, 1997, Eastman wrote to the 22 physicians around the U.S. who were carrying out the NIH's diabetes prevention study, telling them that the British distributor of Rezulin was about to pull the drug.

"This is apparently a marketing decision, rather than a regulatory one," Eastman wrote. The withdrawal was voluntary, but it was made in consultation with officials at Britain's Medicines Control Agency, who concluded that Rezulin was unsafe.

An internal Warner-Lambert document circulated about that time termed Eastman and his NIH colleagues "the strongest advocates for the safety of this drug."

On May 17, 1998, a participant in the major NIH study that Eastman supervised suffered sudden liver failure and died.

The victim was Audrey LaRue Jones, a 55-year-old high school teacher from East St.

Louis, Ill. The death loomed as an indictment of Rezulin because Jones fell into liver failure despite having her liver functions monitored monthly, consistent with the product labeling. Some 580 other patients remained on the drug in the NIH study.

For nearly three weeks, Eastman and his colleagues on the executive committee held off on informing the patients or the other doctors conducting the study about Jones' death, the new documents show.

On June 2, 1998, Eastman and a handful of other NIH officials met in Bethesda with the study's six-member data monitoring board to decide whether to banish Rezulin from the experiment.

Experts retained by the NIH to evaluate the case had found that Rezulin probably caused the woman's liver failure. The death certificate attributed the "underlying cause" to the liver failure.

Newly obtained handwritten minutes of the NIH meeting show that Eastman called the case "unusual" and asked, "Do we want to write off [Rezulin] because of a very bizarre death?"

The board recommended unanimously that Rezulin be removed; the director of the NIH's diabetes institute upheld the recommendation.

On June 4, 1998, 18 days after Jones died, the chairman of the NIH's executive committee informed doctors conducting the study about her death.

"It is possible that you may be contacted by the press," the official wrote. "Please be polite, but refer all questions to Dr. Richard Eastman."

In May 2000, the inspector general's office found that Eastman's arrangements "were reviewed and approved in accordance with the internal NIH regulations."

The investigation report concluded that unspecified "administrative errors ... contributed to the appearance of a conflict of interest associated with Dr. Eastman's outside activities with Warner-Lambert Company."

In June 2000, after nearly a decade on the job, Eastman, whose federal salary was $144,000, left the NIH to join a medical device company based in Redwood City, Calif.

Eastman was not alone in taking Warner-Lambert's money.

At least 12 of the 22 academic researchers selected by the NIH to help conduct the nationwide study received company fees or research grants, according to records and interviews.

The chairman of the study's data monitoring board, responsible for protecting patients from unnecessary risks, also took fees from a Warner-Lambert affiliate.

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CASE STUDY | JOHN I. GALLIN

A Clinic Chief's Desire to 'Learn About Industry'

David Willman

BETHESDA, Md. — Dr. John I. Gallin is director of the NIH Clinical Center — the nation's largest site of medical research on humans.

Thousands of patients go there each year seeking experimental treatments that, if successful, can pioneer new standards of care for all Americans. Drug companies, eager to get new products to market, vie to have their medicines and technologies tested in the NIH research.

This places Gallin and the 600 physicians he oversees in a delicate position: He is an intermediary between the hopes of patients and the ambitions of industry.

Yet Gallin, whose government salary is $225,200, has reported investments in eight biotechnology and pharmaceutical companies. And he received between $145,000 and $322,000 in consulting-related stock proceeds and fees from 1997 through last year, according to his government filings.

The potential for conflicts of interest is raised by Gallin's government positions: He is the Clinical Center director and a leader of the NIH Laboratory of Host Defenses, where he has helped manage gene therapy experiments.

Gallin has filed recusals, pledging not to participate in government decisions affecting the companies in which he has disclosed a financial interest. His outside dealings have been approved by other NIH leaders.

"I thought the experience of working with a biomedical company would give me an opportunity to learn about industry as well as broaden my exposure to current research," Gallin said. "It is necessary that all entities work together to improve the health of the nation."

But taking industry's money, while at the same time avoiding the companies in his NIH role, has proven a challenge, as his dealings with a company specializing in gene therapy, Cell Genesys Inc., show:

In June 1997, Gallin and his lab were completing work on a gene therapy study in collaboration with industry partners. That same month, Cell Genesys acquired one of those partners — a company that had contributed crucial gene-transfer technology.

In July 1997, Cell Genesys made a "demand," according to Gallin: The company wanted the published results of the gene therapy study to identify Cell Genesys as the contributor of the technology — even though it had not performed the work.

Gallin's top lab deputy granted the company's request; Gallin did not object. When they submitted the article to a journal that month for publication, the authors cited Cell Genesys as the contributor of the gene technology. On Sept. 3, 1997, Gallin became a paid consultant to a Cell Genesys subsidiary, Abgenix Inc.

The article appeared in the Proceedings of the National Academy of Sciences in October 1997. Describing the results as "encouraging news," the NIH issued a news release that credited Gallin and his lab for leading the research. At the company's request, Gallin said, the release also cited Cell Genesys for providing the technology.

Gallin made between $132,700 and $319,776 from Abgenix consulting fees and stock-option proceeds from 1997 through 2002, according to his yearly income reports. (He reported payments in ranges, not exact amounts.)

Cell Genesys owned Abgenix when Gallin was hired and held a majority stake in the subsidiary until July 1998, records show. As of last month, Cell Genesys maintained a minority position.

Gallin also became a shareholder in Cell Genesys in 1999, but for two years he did not disclose the holding on his annual financial reports. "It was an error," Gallin said. He sold shares in Cell Genesys last year for $15,000 to $50,000, according to his income report.

In written responses to questions from the Los Angeles Times, Gallin said that when he was hired to consult in 1997, "I was assured by Abgenix staff that Abgenix was an independent company." He added, "I did not consult for Cell Genesys."

In March 2000, Gallin acknowledged the relationship between the two companies. He filed a recusal, saying that "since Abgenix is partially owned by Cell Genesys, I have been advised that an activity with these outside organizations may present an actual or the appearance of a conflict of interest."

Regarding Cell Genesys' requests that it be cited publicly as the contributor of the gene-transfer technology used by his NIH lab, Gallin said that he deferred to his deputy, who was the first-named author on the article.

"I had no involvement other than the first author informed me that this was to be done," Gallin said.

He said agency leaders approved his consulting and stock ownership.

"I was very careful to solicit advice from NIH leadership as to whether or not my accepting the position of serving on the Abgenix scientific advisory board was a conflict that should be avoided," said Gallin, 60, who arrived at NIH in 1971 after graduating from Cornell University Medical School.

Gallin said nearly all of his other investments in biomedical companies were initiated by a financial advisor "in my wife's name, without her or my consultation."

Gallin added, "The stock purchases were not with companies I had any relationship with in my position at NIH. I listed them in my annual [NIH disclosure reports]. If I thought there was a possibility of a conflict I filed a recusal." He said nearly all of the holdings were sold by the end of last year.

Dr. Ruth L. Kirschstein, the NIH deputy director, at first told The Times that she had never allowed an official to own a drug company stock if it required filing a recusal. But Kirschstein later corrected herself, acknowledging that she personally approved recusals that allowed Gallin to own stock in several companies.

For Gallin, avoiding matters involving Abgenix could grow more complicated because of its many new research partners, including industry giants Pfizer, Amgen and AstraZeneca.

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CASE STUDY | JEFFREY SCHLOM

A Cancer Expert Who Aided Studies Using a Drug Wanted by a Client

David Willman

BETHESDA, Md. — While managing one of the National Cancer Institute's major laboratories, Jeffrey Schlom has built a busy outside career as a consultant.

Within a decade, he has accepted fees totaling $331,500 from 20 biomedical companies, his yearly income-disclosure reports show.

The company that paid him the most — $127,000 — was Cytoclonal Pharmaceutics Inc. of Dallas. While Cytoclonal worked on a more efficient way to produce the popular cancer drug Taxol, Schlom helped lead two NIH-funded studies in which Taxol played a crucial part.

Schlom was a co-author of two medical journal articles that reported positive results from that research, conducted at the University of Alabama and published in August 2001 and September 2002.

Taxol was used to enhance the effectiveness of a second cancer drug, developed by Schlom at the NIH.

Schlom's twin roles — as Cytoclonal consultant and NIH leader — posed a potential conflict of interest because the study results could help create more demand for Taxol.

Schlom, in written comments to the Los Angeles Times, said all of his consulting work was done properly, in compliance with NIH rules.

He said he had advised companies "based on my general knowledge and expertise in immunology."

Schlom joined Cytoclonal's scientific advisory board in 1992.

"At our request, the scientific advisors review and evaluate our research programs and advise us with respect to technical matters in fields in which we are involved," Cytoclonal said in various public financial reports, starting in July 1996.

The company repeatedly touted its development of Taxol in news releases.

The company sought to produce Taxol through genetic engineering and fermentation, instead of deriving the drug's active ingredient from the bark of the rare Pacific yew tree.

In June 1998, Cytoclonal entered a licensing and research agreement with Bristol-Myers Squibb Co., the pharmaceutical giant that markets Taxol. Cytoclonal announced that its deal with Bristol-Myers was potentially worth "up to $50 million."

As recently as August 2001, the company, renamed as eXegenics, said that its development of Taxol was one of two projects "with the greatest potential for rapid commercial success."

The company has recently laid off most of its employees and abandoned all research, including the Taxol project.

"We're not seeking to develop it," said David E. Riggs, the company's new chief financial officer.

Schlom, 61, whose government salary is $180,400, has led the National Cancer Institute's Laboratory of Tumor Immunology and Biology since 1982. He supervises nine research groups seeking new ways to treat and prevent cancer.

According to its Web site, the laboratory investigates potential cancer-fighting vaccines. It examines substances, called antigens, that stimulate the body's production of antibodies. And lab researchers design and develop certain "monoclonal" antibodies that show promise in recognizing and targeting cancer cells.

During his decade of consulting for Cytoclonal, Schlom said he "was never involved in any conversations or provided any advice concerning Taxol."

Schlom said he saw no conflict of interest in his role with the NIH-funded studies that reported positive results using Taxol. His involvement related only to the studies' use of a monoclonal antibody developed at his lab, not Taxol, Schlom said.

Yet the studies used both drugs together to treat patients with ovarian cancer.

The antibody developed by Schlom, with a radioactive element attached to it, was given to patients who two days earlier took Taxol.

The researchers had hoped Taxol would make the cancer cells more vulnerable to being damaged or killed by the radiation. The positive results were consistent with other studies that suggested Taxol's value as a sensitizer to radiation.

"I provided expertise only involving the use of the antibody," Schlom said. "Therefore, there was no need for a recusal." Under recusals, NIH employees pledge not to participate in decisions affecting outside clients.

In addition to Cytoclonal, several other companies that have paid fees to Schlom have conducted cancer research:

• Jenner Biotherapies Inc. of San Ramon, Calif., a developer of vaccines for colorectal and prostate cancer, paid Schlom $71,000 from 1993 through 1998.

• AltaRex Corp. of Canada, a developer of antibody treatments for ovarian and other cancers, paid Schlom $17,800 from 1999 through 2001.

• Titan Pharmaceuticals Inc., based in South San Francisco, has tried to develop two monoclonal antibody agents for treating colorectal cancer. Both are being tested in an NIH-funded study. Titan paid Schlom $27,000 from 1996 through 1999.

• Biomira Inc., a Canadian company, is developing an experimental vaccine for lymphoma under a cooperative agreement with another lab at the National Cancer Institute. In May of 2001, Schlom collected a $9,000 consulting fee from Biomira. A spokesman for the company said in November that Schlom was no longer under contract.

Schlom said that he had not, in his NIH capacity, discussed or "promoted any of the studies done by the organizations for which I have been a consultant."

Until last fall, Schlom's ongoing payments from industry were disclosed in annual financial reports open to public review. He now files confidential reports.