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Chemistry Magazine: Where Have Researchers' Ethics Gone?

Where Have Researchers' Ethics Gone?

BY CYNTHIA WASHAM

As pressure increases on scientists to not only publish or perish, but file patents and generate revenues for their institutions, ethical behavior may be getting lost in the shuffle.

Elias (E. J.) Corey (ACS '47) misses the good old days when professors chatted about their research with whoever would listen and studied whatever struck their fancy. They'd never make a million. Then again, they never expected to, either. "There was a premium on ingenuity and self-reliance," says the Nobel laureate, reminiscing about the 1950s and 1960s. "I'm a thrifty New Englander. I had a simple life."

Marcel LaFollette
JOHN BARRAT, SMITHSONIAN INSTITUTION

Today, as he has since 1959, Corey tries to keep life simple at his Harvard University lab. It gets harder every year—there's pressure to produce, pressure to patent, pressure to secure not only the government funding that traditionally supported the lab, but also funding from the private sector. Yet even when presented with the chance to relieve some of that pressure, Corey didn't succumb to the temptations of instant riches.

Earlier this year, Corey had what looked like an opportunity to make a heap of money, for himself and for Harvard. He developed a method of synthesizing the only treatment for avian flu in humans. Corey's synthesis of oseltamivir phosphate is quicker and cheaper than the process used by manufacturer Roche, which sells the product under the brand name Tamiflu. He published his process in the May 20, 2006, issue of the *Journal of the American Chemical Society*.

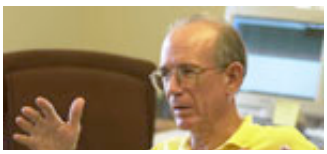
Sheldon Krimsky
TUFTS UNIVERSITY

"We came up with a very efficient route," Corey says. "The yield is twice as much as with the present process."

Harvard could have patented the process. With his share of the royalties, Corey might have been able to look forward to a retirement that isn't quite so thrifty. But he persuaded the university to forgo a patent. "If there were an epidemic of bird flu, I think it's important to save lives and reduce the cost of medicine," he says. "All that is reward enough for me."

That attitude is as up-to-date as bobby socks and poodle skirts. Professors these days jump at the chance to earn more than their modest university wages. They patent their discoveries. They seek out generous research funding from big business. Some moonlight as consultants.

Such practices may be ethical, and some might think Corey to be old-fashioned. But critics fear that such practices create the temptation to engage in other practices that aren't to Corey's standards.



Roadblock to Communication

The abundant opportunities university researchers have to earn money above and beyond their salaries were created only in the past two to three decades. Many

trace the stampede for outside income to the Bayh–Dole Act, which Congress passed in 1980 as an incentive to encourage entrepreneurship and stimulate state and local economies. Bayh–Dole not only allowed but encouraged universities to patent discoveries that their faculty members made with federal funds. Historically, Uncle Sam had the right to patent what he paid for.

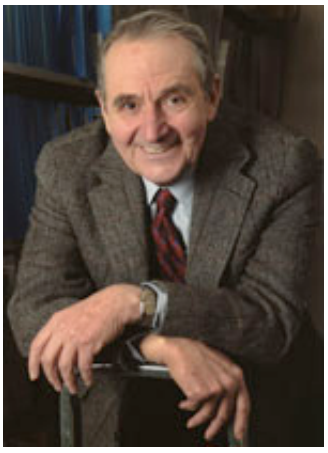
Donald Kennedy
LINDA A. CICERO/STANFORD UNIVERSITY NEWS SERVICE

In the wake of Bayh–Dole, technology-transfer offices started cropping up like hacky-sack balls on college campuses. Universities eager to exploit this new gold mine offered faculty members up to 50% of the royalties on their patents. University presidents dreamed of winning the jackpot, like the University of California did when it was awarded $200 million in a patent-rights lawsuit against Genentech. In reality, most universities earn little more than $1 million a year on patent sales and royalties.

Jim Burkhart
ARNOLD GREENWELL/EHP

"Bayh–Dole turned every gene splicer into an entrepreneur," says Sheldon Krimsky, a professor at Tufts University in Massachusetts and author of the book *Science in the Private Interest*. "Universities began turning themselves into private enterprise zones."

The first casualty of university patenting was candor. Academic researchers have a long tradition of give and take. A researcher collaborates with a couple of colleagues because she knows the study will be better than it would if she had worked alone. Another replicates an experiment he read about in *Organic Letters*, and in the process learns a little more than the authors did. He writes about it, adding to his field's body of knowledge. Such candor disappears among scientists developing the product du jour.



Elias Corey (ACS '47)
HARVARD UNIVERSITY

"Scientists need to be open about their work," Krimsky says. "They need to publish. The entrepreneurial spirit of universities has created a roadblock to communication among scientists."

Corey understands universities' quest for patent income and has even patented a few syntheses himself. Yet he loathes the chilling effect patenting has on researchers. "I like my people to talk openly with one another about what they're doing," he says. "But if you're going down the road of something of great commercial value, you have to worry about public disclosure."

Jumping to Conclusions

If candor is the everyday casualty of patenting, honesty is the catastrophic loss. The most flagrant liars make headlines in *The New York Times*. South Korea's idol Hwang Woo-Suk did in 2005 when he and his team claimed they created the first human embryonic stem cells from several donors' somatic cells. His achievement suggested patients could be treated with tailor-made stem cells with no risk of immune reactions. Hwang had applied for a patent that could have brought him a fortune. That dream ended, and Hwang made international headlines again early in 2006, when officials at Seoul National University discovered his landmark study was made up.

David Goodstein
CALTECH

The ink had barely dried on the stem-cell stories when scientific fraud again made the news. This time, a recently graduated Ph.D. student at New York's Columbia University was suspected of fabricating studies published in the *Journal of the American Chemical Society*. In March, coauthor and chemistry professor Dalibor Sames (ACS '94) retracted two articles and parts of a third he'd published in 2005 with Bengü Sezen (ACS '01). In June, the professor retracted four earlier studies the pair had penned when he determined that they, too, were made up. Had they been reproducible, the studies on manipulating carbon–hydrogen bonds might have led to new types of plastics and drugs.

Neither Hwang nor Sezen have said what drove them to fabricate research or have even admitted to their lies. Ethicists have a pretty good idea, though.

"The pressure to produce results leads researchers to do things they wouldn't do

without that pressure," says Julia Frugoli, an ethics expert and assistant professor of genetics at Clemson University in South Carolina. "If a lot is at stake, it's easy to justify sending a study out for publication and figuring out what's wrong later. It takes a strong person to say the most important thing is to get it right."

David Goodstein, a vice-provost and creator of the policy on research misconduct at the California Institute of Technology, also sees high stakes driving researchers to cut corners. "They think they know how the experiment would come out, but aren't willing to go through all the trouble," he says. "The [lies] start out small and get bigger and bigger until they get caught."

Getting caught is likely given science's publishing tradition. Before a research paper even gets into print, it is normally scrutinized by the editor, then by expert peer reviewers. Some worry that this first safety net in the fraud-detection process is being weakened, though, because trends such as globalization and an increase in electronic publishing have increased workloads for editors and reviewers alike. But that's where the second safety net comes in, since a fraudulent paper that escapes the eyes of editors and reviewers usually is uncovered by readers trying to replicate the results. "The only test of scientific truth is repetition," says Donald Kennedy, editor of the journal *Science*, which published and later retracted Hwang's studies. "The chances of eventual detection [of fraud] are high."

Little White Lies

Made-up studies are so rare they're of little concern to scientists. What worries them are the skyrocketing and sometimes seemingly unavoidable little white lies. Like the big fat lies, they seem to creep into research when the researcher has a financial stake in the results.

Often that stake comes from the deep pockets of big business. When patenting incentives in the 1980s started shifting university scientists' focus from basic toward applied research, industry discovered a ripe pool of talent. "Increasingly, corporations are not doing research inside," Krimsky says. "Labor of postdocs and Ph.D. students is less expensive than people on [a company's] staff. And it has greater status."

Corporate dollars poured into universities, sometimes reaching 25% of their research-and-development budget. California's Stanford University led the country in private funding in 2004–2005, with $6.04 million. The University of Wisconsin at Madison ranked second, with $5.95 million, followed by Harvard University, with $5.90 million.

The missing link? For 40 years, people thought so, until it was revealed in 1953 that Charles Dawson assembled his Piltdown Man fossil from a human skull, an orangutan jaw, and animal teeth.

Even the great Sir Isaac Newton sometimes cut corners. Historians have discovered that Newton cooked some of the data on the precession of equinoxes and the velocity of sound. Luckily for him, his theories were still correct.

James Visintainer
(ACS '79)

Julia Frugoli
CLEMSON UNIVERSITY

For those who've earned the right to call themselves scientists, the funding source shouldn't matter. Scientists are trained to be objective observers regardless of who's footing the bill. Yet studies of sponsored research paint a different picture.

The *Journal of General Internal Medicine* reported in January 2004 that authors with a conflict of interest were 10–20 times less likely to report negative findings in a study than those without. The study was based on articles published in the *Journal of the American Medical Association* and the *New England Journal of Medicine*. And in a survey published in the June 9, 2005, issue of *Nature*, 15% of 3,000 government-funded scientists admitted they changed a study's designs or results to satisfy a sponsor.

"Conclusions of privately sponsored research are more likely to support the financial interest of the sponsor, compared to similar research funded by not-for-profits or public funding," Krimsky says. "Data can have different interpretations. Investigators funded by private sponsors give the most favorable interpretation."

The textbook example of industry's control over scientific research is the body of published literature on the health effects of second-hand smoke. Around the late 1980s and early 1990s, public-health officials warned that exposure to other people's cigarette smoke could cause cancer and heart disease. Tobacco companies responded by establishing the nonprofit Center for Indoor Air Research. Over the next 10 years, the scientific-sounding center funded at least 244 seemingly independent studies, all refuting the U.S. Environmental Protection Agency's warning that second-hand smoke can cause cancer and heart disease.

Slipping through a Loophole

Like their colleagues in academia, government scientists also fall prey to conflicts of interest. The *Los Angeles Times* in 2003 and 2004 ran a series of articles exposing secret deals between government scientists researching new drugs and the companies making those drugs.

One of the series' most notorious targets was the National Institutes of Health's (NIH) top diabetes researcher, Richard Eastman. In 1996, Eastman hailed Warner-Lambert's new drug Rezulin for its ability to correct the underlying cause of diabetes, although that effect was never proven. Physicians prescribed the drug to more than a million patients. Troubles began surfacing in 1998 when a woman enrolled in a clinical trial died from liver failure. The U.S. Food and Drug Administration (FDA) since linked the drug to 738 adverse reactions, including serious liver damage and 33 deaths.

Physicians prescribing Rezulin didn't know then that while Eastman was supervising the NIH study, he also was working as a consultant for Warner-Lambert. The drug company paid him $78,455, according to the *Times*. The *Times* reported that at least 12 of the 22 academic researchers chosen by the NIH to study Rezulin also received payments from Warner-Lambert. In 2000, the company pulled Rezulin from the market at the FDA's request.

Congressional hearings in 2004 uncovered dozens of examples of conflicts of interest and outright corruption in the NIH. Investigators found that only 100 of 264 arrangements between NIH scientists and pharmaceutical manufacturers had been reported to the NIH as required. Gary Nabel, director of the vaccine center, told Congress that he and 80% of his critical researchers moonlight for the drug industry. He said he could not attract

the best scientists without offers of lucrative outside work.

In the two years since the hearings, NIH Director Elias Zerhouni claims his employees have cut their ties to drug and biotechnology companies. The NIH now bans nearly all outside work. Zerhouni says NIH workers also are complying with a new requirement to disclose personal investments in medical companies.

Like the NIH, the FDA prohibits its employees from accepting money, gifts, or trips from the companies it regulates. But a report from the Center for Public Integrity, published last March, showed how employees are slipping through a loophole. The nonprofit Drug Information Association and several similar organizations of drug manufacturers pay for FDA employees' trips. According to the report, five associations spent more than $1.3 million on 1000 excursions for FDA employees over a period of six years.

Sins of Omission

If editors can't control the source of their authors' funding, they can at least require authors to disclose it. "Disclosure is good for all parties concerned," says James Burkhart, acting editor-in-chief for *Environmental Health Perspectives*.

Professional journals typically ask authors to disclose conflicts. Some critics wonder, though, if disclosure policies go far enough. For example, one study released in July 2004 by the Center for Science in the Public Interest found that 8% of authors who had conflicts of interest failed to report them. One of them was Hwang. According to a January 18 article in *Nature*, the stem-cell researcher concealed the fact that he had applied for a patent on a process he published in 2004.

Had he written for *Environmental Health Perspectives*, he would have been banned from publishing in the magazine for three years, even if his study had been honest. The magazine has one of the publishing industry's most stringent disclosure requirements. "We felt we needed to put teeth into it," Burkhart says. "I think just by having it there, people are more cognizant of their obligation to come to full disclosure. Transparency is the best thing for everyone."

The *New England Journal of Medicine* once prohibited its drug reviewers from accepting any compensation from drug companies. Editor Jeffrey Drazen overturned that policy in 2002, saying he couldn't find enough reviewers without industry ties. To minimize bias, he limited reviewers to $10,000 per year in speaking and consulting fees from each drug company.

Dipping and Clipping

Moonlighting, concealing a conflict of interest, slanting a report to please a sponsor—all of these practices fall into the gray zone of science ethics. One scientist might get fired for it; another might get promoted. When it comes to ethical breaches, researchers have only three upon which they universally agree—fabrication, falsification, and plagiarism. Rare as the first two are, the latter is alarmingly common. In one particularly egregious case, 21 mechanical engineering graduates of Ohio University were found to have plagiarized their master's degree theses.

Kent State University physics instructor James Visintainer used to have his students write essays outside of class. He stopped that practice when he realized many were plagiarized. "Many students feel that if they find it on the Internet, they can use it without citation," Visintainer says. "I think it's part of their nature to think it's theirs."

Marcel LaFollette saw the same guiltless electronic looting in her students. "Computers have made it so easy for kids to steal words," says LaFollette, a former professor of science policy and author of the book *Stealing into Print: Fraud, Plagiarism, and Misconduct in Scientific Publishing*. "If you see the web as one great pool of information into which you dip and clip, how can I as an instructor say don't do that in my course, when all your life, that's the way it was?"

LaFollette realized just how rampant plagiarism is when she came across an editorial on plagiarism that had been plagiarized from an article she'd written. "I have yet to talk about plagiarism to someone who hasn't had something stolen," she says.

The Pendulum Swings

So who's going to teach scientists when it's okay to copy? (When they give the author credit.) And when it isn't? (When they don't.) Who will tell the Dow-funded researcher if she needs to disclose that Dow stock is in her mutual funds? (She doesn't.) Or if it's OK to throw out the one set of data points that's way off the curve? (Only if the experiment was botched.)

Scientists historically resisted anything resembling rules. “Scientists don’t like people telling them what to do,” Frugoli says. “They say they can police themselves.”

That’s long been the thinking at the ACS. Outside of the Society's publishing guidelines, the 130-year-old organization addresses ethical issues in two publications - the *Academic Professional Guidelines* and the *Professional Employment Guidelines* - as well in the *Chemists Code of Conduct*. The code urges chemists to ensure that their research is “thorough, accurate and unbiased” without giving an explanation of what unbiased means. “Chemists have responsibility to avoid pollution and to protect the environment,” the code advises, but it doesn’t tell readers how.

For some, though, this code just wasn’t enough. “Members wanted a place they could go for guidance on ethics issues,” says Eric Slater, the ACS’s copyright manager and staff liaison for the ACS Committee on Ethics. That committee met for the first time in March 2006. “We want to take leadership in educating members about ethics,” says Marge Cavanaugh (ACS ’72), committee chairwoman. “We hope to promote high standards of ethical conduct.”

She envisions the committee creating an ethics section on the ACS website, possibly including case studies that members can discuss online. Cavanaugh also expects the committee to raise ethical issues in the ACS journals. Another one of her goals is to recognize members who are ethical role models. (*Chemistry* will be introducing a regular ethics column beginning with the Spring 2007 issue.)

Can Cavanaugh and her committee rescue an image tarnished by fabricated studies and scientists on the take? Ethics observer Krimsky is skeptical. “You see a decline in the ethics of science,” he says. “The objective scientist is a dying breed.”

Still, he hasn’t given up on men and women in white lab coats. “Awareness [of ethics] is up,” he says. “Transparency is up. But the root of the problem is still there. I can still be hopeful there’s the beginning of a pendulum swing.”

Cynthia Washam is a freelance writer who lives in Jensen Beach, FL. She wishes that all professionals paid as much attention to ethics as do scientists.

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