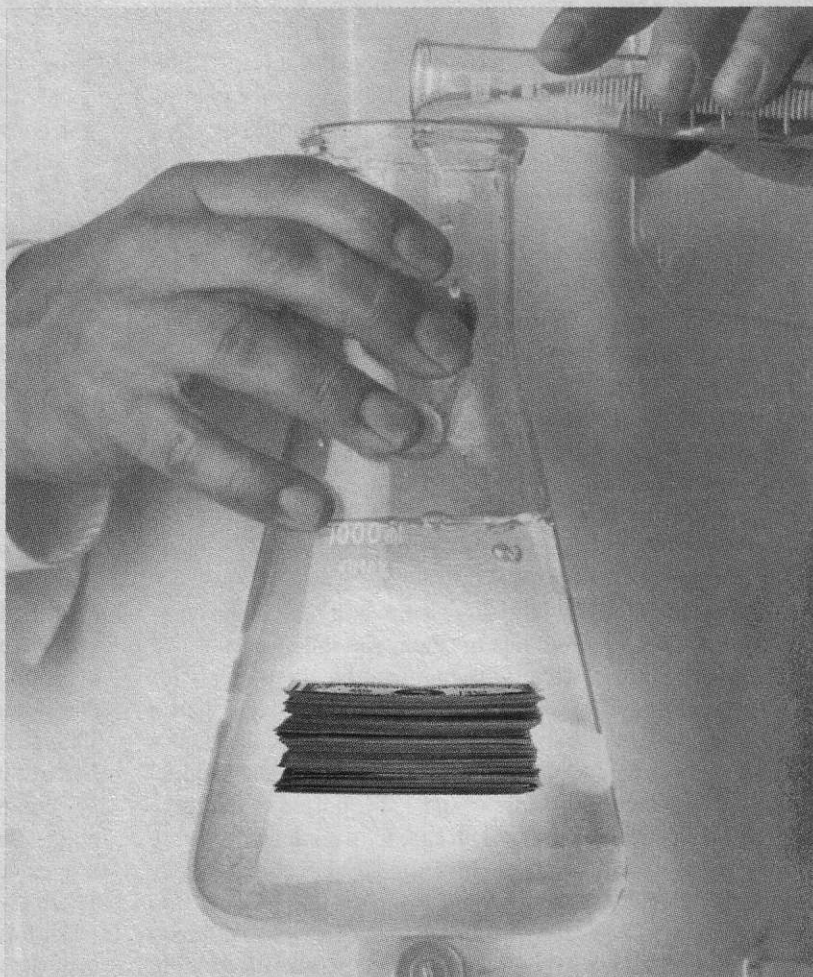


## ARTICLES

# Money + Science = Ethics Problems on Campus

by DAVID SHENK



The third most dispensed drug in the United States is a thyroid medication called Synthroid. Eight million Americans suffering from hypothyroidism take Synthroid every day, paying a premium for Knoll Pharmaceutical's top-selling brand name rather than buying the much less expensive generic alternative. As is the case with most brand leaders, Knoll's enormous success with Synthroid is entirely dependent on its continuing ability to convince its users and the healthcare community that its drug is worth the extra cost. This the company has done brilliantly for decades, despite any real proof of Synthroid's superiority.

In the late eighties, the company (then known as Boots Pharmaceutical) had good reason to believe it was on the verge of obtaining such proof. A clinical pharmacist at the University of California, San Francisco, named Betty Dong published a limited study that strongly suggested Synthroid would beat out its competitors in a blind, randomized trial. The company approached Dong, offering her the full \$250,000 needed to pay for such a long and complex study.

Alas, the study backfired on the company. To the surprise of nearly everyone, including Dong, the results suggested that Synthroid was no more or less effective than three much cheaper

competitors. All four were what scientists call "bioequivalent."

But the company had a trump card. As the study's sponsor, it had not only been able to design the protocols of the drug trial; it also had exclusive access to the prepublished results of the study as well as final approval over whether the study could ever be made public. Not surprisingly, with the results so threatening to its marketing efforts, Knoll set out to thwart the study. In addition to delaying its publication in a scientific journal by many years, effectively destroying the relevance of its data, the company also undermined the study's message by pre-emptively publishing the UCSF data in a different journal with a different (much friendlier) conclusion. Then Knoll waged a massive PR campaign against the real study, "Bioequivalence of Generic and Brand-name Levothyroxine Products in the Treatment of Hypothyroidism," by Betty J. Dong et al., after it was finally published in the spring of 1997 in the eminent *Journal of the American Medical Association (JAMA)*.

A massive class-action lawsuit followed the publication of Dong's *JAMA* report, alleging on behalf of all Synthroid users that Knoll had defrauded them of hundreds of millions of dollars in inflated costs. The company has offered to settle for a sum close to \$100 million—which would be the largest cash settlement for a class-action suit of its kind in history. And yet, even with such a fantastic price to pay, one can only conclude that in the end Knoll has benefited tremendously from its brash interference in the academic research process: A hundred million is but a small fraction of the profits the company made from Synthroid during the years it was suppressing the study. And by its ability to taint Dong's study with controversy over the years, Knoll was able to nullify any would-be effect. "Sales continue to grow very rapidly," Carter Eckert, Knoll's president, told me when I visited him at the company's rural New Jersey headquarters. "Our position has been validated."

Betty Dong's case, while extraordinary, is not isolated. In Toronto, liver specialist Nancy Olivieri was threatened with legal action by the Canadian drug giant Apotex if she published criticisms of its drug L1, concerns that had emerged from a clinical trial the company was sponsoring. In Providence, Rhode Island, Brown University's director of occupational medicine, David Kern, was pressured both by a local company and by his own university not to publish his findings about a new lung disease breaking out at the company's plant (Kern did publish his data, and the disease Flock Worker's Lung was officially recognized by the Centers for Disease Control in September 1997). In Winston-Salem, North Carolina, hypertension expert Curt Furberg and three colleagues resigned from a major Sandoz-funded study of calcium channel blockers, a controversial class of drugs purported to decrease the risk of heart attacks, rather than cave in to company pressure to spin negative results in a positive light. "I have seen people in industry asking for stranger and stranger things in private funding, as far as control is concerned," says Gregory Gardiner, Yale's senior director of the Office of Cooperative Research. Indeed, these sensational cases may well be only the visible tip of a broader crisis in academic science. Over the past two decades, university-industry partnerships have become a ubiquitous feature of biotech research, and with this new closeness has come a raft of new concerns about whether the soul of academic science is being slowly eaten away. "We need to be vigilant," suggests Gardiner, "to make sure nothing is happening to university science."

The infusion of private capital is staggering. In 1997 US companies spent an extraordinary \$1.7 billion on university-based science and engineering research, a fivefold increase from 1977. More than 90 percent of life-science companies now have some type of formal relationship with academic scientists, and 60 percent of those report that they have achieved new patents, products

and sales as a result. In the realm of university science, at least, that once-remote ivory tower now finds itself cater-corner to an office park—in many cases literally.

No one doubts that this surge in university-industry alliances has produced enormous scientific progress, yielding important new drugs like the anti-HIV agent 3TC, a synthetic version of the anticancer drug Taxol and the Haemophilus b conjugate children's vaccine for bacterial meningitis. University-industry alliances have also hatched many critical tests and medical technologies, prolonging and improving countless lives.

The new alliances have also generated a lot of profit. According to the Association of University Technology Managers, a boosterish pro-alliance trade group, corporate licensing of university inventions now accounts for \$21 billion in annual revenue, which in turn supports 180,000 jobs. The arrangement has also become an important new revenue stream for academic institutions and for individual faculty: In fiscal year 1993 the top ten universities alone received \$170 million in product royalties. In the majority of campus technology transfer policies, the researchers making discoveries are entitled to a portion of that money. Sure enough, a survey by Tufts University's Sheldon

Krimsky of articles published in 1992 in the fourteen leading US biomedical journals disclosed that 15 percent of lead authors had some significant financial interest in their

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published report. A similar survey in 1996 suggested the proportion was closer to one-third. And a just-completed Krimsky study of 62,000 articles published in 210 different journals revealed that potential conflicts-of-interest are almost never reported. Though all 210 journals have a formal disclosure requirement, 142 of them did not publish a single disclosure in all of 1997. "Companies say, 'Here's the design. Are you interested?'" explains Bowman Gray medical school's Curt Furberg. "Being interested means a lot of funding for you and your institution. There's a lot of appeal in going along."

Unfortunately, the cost of economic success may often be the integrity of the science itself. What are we to make of a recent study published in *JAMA* suggesting that an astounding 43 percent of women and 31 percent of men suffer from "sexual dysfunction"—once we also discover that two of the study's authors served as paid consultants to Pfizer, which manufactures Viagra? (The relationships were not disclosed in *JAMA*.) If individual researchers are profiting from their own research, considers University of Pennsylvania bioethicist Mildred Cho, "the outcome or direction of their work may be affected. They might, for instance, be tempted (consciously or unconsciously) to design studies that are more likely than not to have an outcome favorable to the product." Or they might be tempted to keep lifesaving but potentially profitable information secret from the colleagues—now competitors—who could most readily build on the discovery. "There is little question that academic faculty have a very different and less critical attitude toward a specific company if they are getting a lot of money," insists Public Citizen's Sidney Wolfe. "It's not just research grants. A number of these people supplement their income by going around the country giving talks funded by the drug