Conflict-of-Interest Spurs New Rules, Not Consensus

Drug manufacturers spent $7.8 billion in 2004 influencing physicians. That works out to roughly $10,000 for every practicing doctor in the country, according to IMS Health, the company that monitors the industry's finances.

They gave gifts, lucrative consulting contracts, and meals; they subsidized doctors' professional conferences and advertised in their journals. They gave drug samples to physicians that were worth another $16 billion.

Now several major research universities and government institutions are setting new rules that limit researchers' contact with pharmaceutical representatives. The policies range from extremely strict, like Stanford University's new "no pens or pizza" policy that limits all gifts no matter the size, to less stringent arrangements that allow doctors to accept drug samples, consult for companies, or own limited amounts of stock in companies that fund their research.

A conference on conflict of interest at the Cleveland Clinic in September outlined many of the still-unresolved issues. Although a few researchers claimed that new restrictions are unnecessary, many others said that separating research from company influence is essential to maintaining research integrity and restoring the public's confidence in major medical centers.

Darel Kirch, M.D., president of the American Association of Medical Colleges in Washington, D.C., said that discussing these issues is important because universities are currently unable to deal with industry-academic conflicts effectively. "We're in uncharted territory," he said. "We need a roadmap."

The Pharma Problem

The value of the money and freebies pharmaceutical manufacturers dish out each year to persuade American physicians and patients to use their drugs is skyrocketing. In 1998, it totaled $12.7 billion. By 2004, it had more than doubled to $27.8 billion. Pharmaceutical companies are not only spending escalating sums of money influencing physicians but also finding new ways to do it. This spring, for the first time, some drug companies paid professional organization dues for doctors finishing their residencies and invited graduating medical students to lavish dinners to begin the relationship even earlier than before, said Claudia Adkison, J.D., Ph.D., the executive associate dean at Emery University School of Medicine in Atlanta.

Phillip Pizzo

The more money that the pharmaceutical industry spends promoting drug sales by winning physicians' allegiance, the more important it becomes to ask whether American doctors are prescribing the best drugs available or merely the ones industry's money talks them into, said Stanford Medical School Dean Phillip Pizzo, M.D., and others. Is the corporation–physician relationship harming patient care?

According to a 2003 article in the *American Journal of Bioethics*, the more interaction physicians have with the drug representatives that give them drug samples and other gifts, the more those physicians prefer "new products that hold no demonstrated advantage over existing ones." Likewise, the more interaction physicians have with drug representatives, the less physicians prescribe generics, the more they prescribe irrationally and incautiously. The result: higher drug costs.

No Gifts, No Visits

Despite the growing interest in fixing conflict of interest, a look at the conflict policies at several American university medical centers shows that they are still a long way from reaching a national consensus on the right rules.

Yale University in New Haven, Conn., the University of Pennsylvania in Philadelphia and—starting in October—Stanford prohibit their physicians from accepting gifts from the medical industry, no matter how small. They also ban drug representatives from patient-care areas.

Although all three universities ban gifts, Yale allows physicians to accept drug samples, provided they give the samples to patients. Stanford's doctors can take freebie drugs, but they must go straight to its pharmacy, where they are distributed to poor patients.

The "no pens or pizza" policy struck many physicians at the conference as overkill, and that view might be more widely held. For example, a survey of 211 American obstetrician/gynecologists published in the *Journal of Medical Ethics* this year found that only one-third agreed that free drug samples influence what drugs they prescribe. It might be in that spirit that the National Institutes of Health recently decided that its employees may receive up to $25 in value per gift or free meal.

But the evidence on the effects of small gifts is counterintuitive, said bioethicist Arthur Caplan, Ph.D., of the University of Pennsylvania and a coauthor of the *Bioethics* article. "Everybody in marketing, everybody in every business school we looked at said that the most powerful gifts were the small ones presented over time," he said. Small gifts work best, Caplan theorizes, because they come in "under our radar," whereas big gifts automatically warn us to put up our conflict-sensing antennae. Pizzo cited one example of the power of small gifts: Former President Lyndon Johnson gave voters toothbrushes with his name on them because "he wanted people to think about him morning and night."

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The Bigger Game

The bigger problem might be the financial interests that physicians and hospitals hold in biotech companies that market drugs and devices they invent, conference attendees said. Since the 1980 Bayh–Dole Act made it legal for doctors and their institutions to profit from those inventions, industry–researcher relationships have proliferated. Gail Cassell, Ph.D., a vice president at Eli Lilly in Indianapolis, said that's why one-third of the nation's 4,000 biotech companies are located within 35 miles of a university campus.

Another reason that academia–industry collaborations have proliferated is that universities need the money more than ever before, several speakers said. Reimbursements for medical services have dropped so much that patient care can no longer pay for physician education at many universities. Kirch said that the increasing privatization of higher education has forced even land-grant universities to find private support.

Because universities share in the profits their researchers' inventions earn, the universities encourage individual researchers to develop as many ties to industry as possible, and those ties become increasingly important to their institutional bottom lines. With so much money being made, researchers become more likely to engage in conflicts, and their universities become less likely to intervene to stop them. Pizzo and others said this is one of the major reasons why some universities have decided they must face the problem of industry–academia conflicts head on, by managing potential conflicts of interest more diligently.

Harvard University's conflict-of-interest rules focus on research involvement with industry, not on drug promotional activities. Faculty can make up to $20,000 per year consulting for a business, but they generally cannot conduct clinical research for that company if they hold stock or executive or board positions in the company. By contrast, Johns Hopkins allows its faculty to conduct clinical research for publicly traded companies, provided that the faculty own no more than $25,000 of company stock and have the medical school's approval. Faculty may not receive royalties from the commercialization of research results, but they can receive book royalties.

The Cleveland Clinic's own conflict-of-interest rules never came up for discussion at the conference, in part because they had been private and unpublished until several days before. Their policy, which is now posted on the Cleveland Clinic Web site, focuses on industry relationships. Staff members are allowed to consult with industry and, with permission, to serve on the boards of companies. They are not allowed to own stock in non–publicly traded companies that sponsor clinic research, but individuals can own up to $10,000 of stock in publicly traded companies.

Cleveland Clinic spokesperson Eileen Sheil said they held the conference "to initiate a national discussion on best practices in conflict-of-interest practices in health care." However, none of the sessions dealt with the clinic's own well-publicized conflicts with industry.

Disclosure Discussion

Discussion at the conference revealed that many universities already require their researchers to disclose potential conflicts of interest in writing once a year. Administrators see it as a way to minimize conflicts, reasoning that most researchers would prefer to disclose than to take the chance of getting caught later.

"Everywhere we've been able to build compliance into activities, we've actually improved our performance," said Edward Miller, M.D., dean and CEO of the Johns Hopkins School of Medicine.

Some participants found disclosure rules unlikely to deter a motivated perpetrator, who would just not disclose his conflicts. Thomas Stossel, M.D., a hematology professor at Harvard, argued that any rules beyond mere disclosure or punishment for nondisclosure are counterproductive, unfair, and unsupported by evidence. "Allegations of harm arise from conjecture and very few anecdotes," Stossel said. "They provide no evidence that more adverse outcomes arise from commercial influence than in its absence."

At a minimum, physicians with a financial stake in companies should be barred from conducting clinical research on that company's products, proposed Paul LaViolette, the chief operating officer of Boston Scientific in Natick, Mass. "A major investor should never have a role in data collection," he said.

Former Merck CEO Roy Vagelos, M.D., said that responsible leadership can prevent conflicts. In the mid-1980s, Merck was eager to get lovastatin (Mevacor) on the market, because "it was lowering cholesterol like nothing ever seen before," he said. But because of rumors that a competing Japanese drug already on the market caused cancer in laboratory animals, Vagelos held lovastatin off the market for another 2 years while Merck conducted toxicology studies to prove that it did not cause cancer.

Moral leadership like this is necessary but "grossly insufficient" to prevent conflicts of interest, said Ed Soule, Ph.D., a certified public accountant turned moral philosopher and business professor at Georgetown University in Washington, D.C. Nor do conflict-of-interest rules alone work well, he said, because research shows that increasing efforts to improve compliance yields diminishing returns.

What is necessary, Soule said, is to build an ethical culture into academic medical centers, something that is usually most successful right after scandals that clean house at an institution and install new, reform-minded leaders. "Culture eats compliance for breakfast," he said. But as attractive and permanent as that idea sounds, he said, culture is not a sure-fire fix because it is "incredibly unstable" and thus extremely difficult to maintain over the long term.

Despite the new ideas and years of discussions that proceeded them, American universities are nowhere close to fixing their conflict-of-interest problems, Caplan said. "We need a national blue-ribbon panel to go at the conflict-of-interest issue in a series of meetings, he said. "The kind of response that's taken place so far, I think, is not up to the level of the problem."

—John Dudley Miller

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