Academia and the company coin

As the economic downturn chokes spin-outs from academia, a spate of newly minted university-industry partnerships are springing up. Failing to address the financial conflicts in such partnerships could spell trouble for both faculty and drug companies. Jim Kling investigates.

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In recent weeks, Massachusetts has been the center for a storm of controversy concerning academia's relationship with industry. Early in March, a grassroots movement involving hundreds of Harvard medical students demanded that the university reform the way it monitors and controls money the school takes in from the drug industry[1] (**Fig. 1**; **Box 1**). Shortly afterward, federal prosecutors alleged that a Massachusetts General Hospital psychiatrist had become a "star spokesman" for a pharmaceutical company, promoting its drugs for treating depressed children even though the medications were not approved for pediatric use[2]. Later the same month, state heath officials gave final approval to regulations banning pharmaceutical and medical device companies from providing gifts to physicians, and requiring companies to publicly disclose payments to doctors over $50 for consulting and speaking engagements[3]—the strictest such regulations in the nation.

The state's difficulties, bellwethers for other research-intensive academic institutions, come on the heels of continuing increases in the number of relationships between drug companies and universities (**Table 1**), driven by thin drug company pipelines, shrinking university endowments and essentially nonexistent federal funds for translational research.

And then there's the US Congress. Last summer, staffers for Iowa senator Charles Grassley found that conflict of interest disclosures by three Harvard psychiatrists vastly underreported millions in payments from drug companies[4]. The investigation swept up the American Psychiatric Association and its president-elect, Stanford's Alan Shatzberg. Although Shatzberg had disclosed his nearly $5 million in drug company stock to the university, the firestorm laid bare how deeply entwined companies and academic scientists have become. Shatzberg, as well as Brown University's Martin Feller and Emory's Charles Nemeroff, have all stepped aside from leadership positions as a result of the Grassley probe.

Pros and cons

The interplay between academia and industry presents a complex ethical landscape, as relationships can take various forms. There are industry-sponsored research agreements, seed venture funds, industry fellowships, support for continuing medical education, intellectual property (IP) deals, equity stakes, free drug samples, even pens and other freebies: every possible arrangement—and not all carry the same weight.

Senators Charles Grassley (R-IA) and Herb Kohl (D-WI) reintroduced their Physician Payments Sunshine Act on January 22. The legislation requires drug companies to report gifts to physicians of $100 or more. Image courtesy of the Office of Senator Grassley.

Two 'hot spots' draw particular concern: interactions that involve patients, such as sponsored clinical trials, and institutional agreements in which corporations provide money in exchange for IP rights and other considerations. Some observers raise concerns that such gifts will make physicians more likely to prescribe a benefactor's drug; and some social science research backs that up. Studies show that people find it difficult to remain objective when they are recipients even of small gifts and even when there are no stated 'strings attached'.[5] In one study, 61% of physicians reported that promotions don't influence their practice—but only 16% believed that the same was true of other physicians[6].

Critics of institutional agreements maintain that such agreements can interfere with academic freedom because companies may restrict publication of research results or encourage secrecy, whereas supporters point to the importance of industry funding and to increased productivity among some recipients of industry money.

David Blumenthal, a professor of medicine at Boston's Massachusetts General Hospital who has researched academic-industry connections, finds that painting all collaborations with industry as potentially restrictive is an oversimplification. "People with modest amounts of industry funding publish more. Those who get almost all their money from industry publish less," he says.

But there are other negative consequences. There have been reports of industry sponsors seeking to suppress or delay the publication of unfavorable data, as well as selectively publishing positive results[7]. Studies also suggest that clinicians with industry ties are more likely to prescribe the companies' brand-name drugs than generics[8,9].

Clinical trials and tribulations

Medical schools are one flashpoint because of concerns over the welfare of clinical trial participants. According to a recent study, some schools have been slow to introduce comprehensive institutional conflict of interest (ICOI) policies, despite the recent availability of examples to follow[10]. Federal regulations were outlined in 1995 to govern conflicts of interest in Public Health Service–funded research, and the Association of American Universities and the Association of American Medical Colleges followed with its own policy guidelines for individual researchers.

Of 86 US medical schools surveyed, only 38% reported having adopted an ICOI policy for financial ties held by the institution. Thirty-seven percent said they were working on one, whereas the remaining 25% reported no plans to adopt such guidelines. Seventy-one percent of respondents had ICOI policies in place for senior officials (deans and vice deans) and 80% reported them for mid-level officials (department heads).

The authors suggest that the increased percentage of institutions with policies governing the behavior of officials is a nod towards the importance of managing conflicts of interest in those overseeing research involving human subjects. Still, about 20% of medical schools lack significant oversight of these officials.

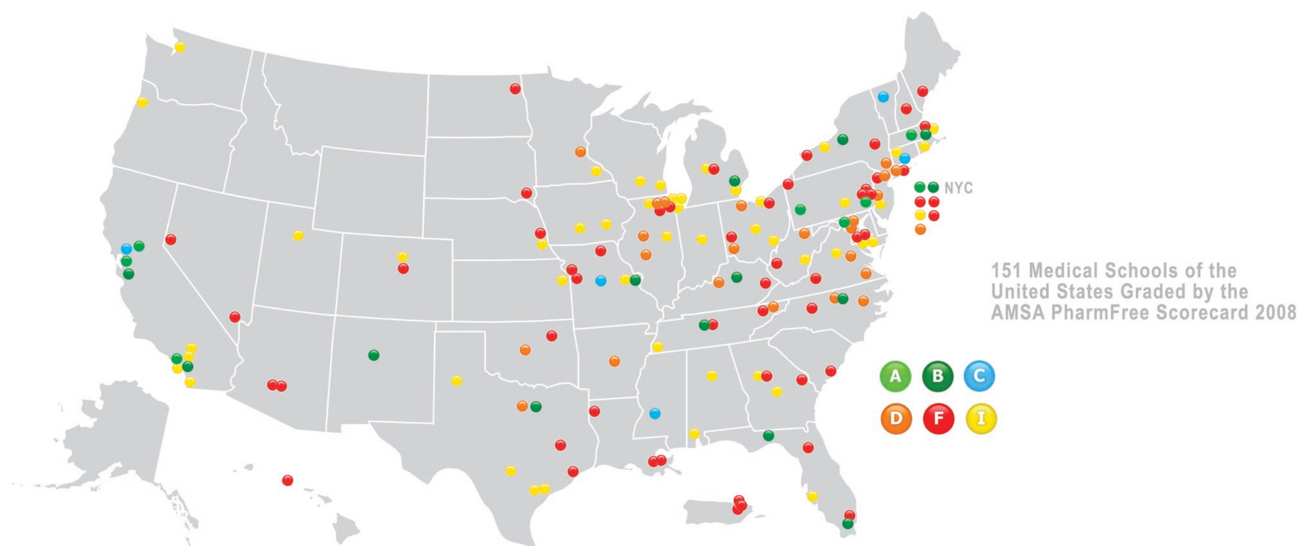

Figure 1 Students give most universities a failing grade. The American Medical Students Association evaluated conflict of interest policies in 151 US medical schools. The largest group (52 out of 151, or 34%) received an F, with only 5% (8) receiving an A. The map reflects data collected in 2008. Some schools have upgraded their scores since then. (Source: Gabrielle Cosel The Pew Prescription Project.)

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The lag in adoption of ICOI policies could be caused by several factors, according to the study's authors. Many medical schools are part of larger universities and may lack the authority to adopt independent policies; insufficient data on actual conflicts may prevent officials from assessing institutional conflict and supporting ICOI guidelines; and such guidelines may be perceived as likely to delay the commercialization of economic research at a time of economic pressure to develop products.

"There are big holes in who has to disclose on the faculty side and what they have to disclose. It's by no means comprehensive or consistent, and it's also not at all consistent what universities do with that information. The whole issue at the faculty level is by and large chaos in the academic setting," says Eric G. Campbell, a professor of health policy at Harvard Medical School in Boston and a coauthor of the study.

In some cases, the problem may be that industry is taking over more study designs and doing so with marketing in mind. "It's about 'How can we broaden out the uses of this drug, how can we promote it among more populations'…studies are marketing designs rather than public health designs. It doesn't advance the body of evidence-based medicine in this country," says Jennifer Washburn, author of *University, Inc.: The Corporate Corruption of Higher Education* and a fellow at the New America Foundation in Washington, DC.

"This has been left to institutions to manage for a very long time, and they've demonstrated that they can't manage these conflicts. I think [self-regulation] is coming to an end," says Campbell, citing the Physician Payment Sunshine Bill introduced by Grassley, and the Prescription Project (http://www.prescriptionproject.org/about/), a Boston-based advocacy group, aimed at eliminating conflicts of interest caused by drug marketing practices, among other state and national efforts.

But some say the problem has been exaggerated. "It's astonishing that there have been so few substantive events that you can come close to blaming on a conflict of interest. It's not even in the same galaxy as Medicare fraud," says Tom Stossel, a professor of medicine at Harvard Medical School. He doesn't deny that there can be problems, but he believes the advantages of industry interaction are too often overlooked. "If you're going to do a risk assessment, you've got to do a benefits assessment. All I'm saying is there should be some flexibility and nuance [in conflict of interest rules]," he says.

Working solutions?

Some universities are proactively restricting industry influence. The University of California, San Francisco (UCSF) has long had stringent rules regarding clinical trial sponsorship: investigators can't receive funds directly from a company while they are conducting clinical trials on the company's drugs. They can own stock, receive honoraria and serve on scientific advisory boards before or after running a sponsored trial, but not during.

UCSF's restrictions have caused some grumbling among its faculty, says Kirby Lee, an assistant professor of clinical pharmacy at the UCSF School of Pharmacy. "It's hard for them to collaborate with industry. One or two have left the university altogether, and others have figured out other ways to collaborate with industry that are maybe not as fruitful as they would like," he says.

Other universities have adopted similar policies, says Lisa Bero, a professor of clinical pharmacy and health policy at UCSF and chair of the chancellor's advisory committee on conflicts of interest. UCSF's policy was strenuously resisted by "a vocal few…who didn't want to give up their financial ties to companies. They felt it would discourage funding of clinical research at UCSF, but we haven't seen that happen. You can still collaborate with companies, and we haven't seen a decline," she says.

A few industry representatives have complained about the policy, Bero adds, but they're often small biotech or device companies that either work with just a few investigators whom they want to pay as consultants or have a faculty member who is a cofounder or owns a significant amount of stock. "It's their company, so they feel that [the particular investigator] is best qualified to do the research because they helped develop the product and were involved in the invention," says Bero.

Part of the issue is that there are often a few noted academic experts who are called on regularly to be on speakers' bureaus or to testify to a Food and Drug Administration panel. And because they are thought leaders, they are often approached by industry for consulting or research collaborations. "It's the same people over and over again," says Stanford University ethicist Mildred Cho, who has studied the impact of university-industry relationships on biomedical research.

Stossel isn't convinced that academia-industry partnerships pose a significant problem. He believes that much of the current brouhaha can be traced to editors of prestigious medical journals: "They've gone on a power trip. They've decided to save medicine against the evil companies…The long, boring, anonymous drudgery of researchers inventing things, of companies creating formulations and [running] clinical trials—that's not news. But the occasional evidence of malfeasance or inadvertent error gets blown up into the tip of the iceberg of a vast conspiracy of corporate greed. The media loves it."

Stossel believes the problems are exacerbated by the industry's subdued response. "Its silence and appeasement conveys the sense that it has something to hide. Compliance bureaucrats and attorneys tell them to just hunker down, and as a result it just goes from bad to worse," he says.

Table 1 Selected partnerships between universities and big pharma

Company	Date	Partner	Deal
AstraZeneca	October 2008	Columbia University Medical Center	Study of neurogenesis with respect to depression and anxiety
	June 2008	Columbia University Medical Center	Study of metabolic diseases, obesity and type 2 diabetes
GlaxoSmithKline	June 2008	Immune Disease Institute	$25 million over five years for joint research projects on immunoinflammation
Johnson & Johnson	November 2008	University of California, San Diego	Research, education and training collaborations with a focus on new clinical applications
Merck	September 2007	Harvard University	Funding for six labs in oncology and central nervous systems disorders
	April 2008	Harvard University	Funding for two labs working on osteoporosis
Pfizer	January 2008	Washington University, St. Louis	$25 million over five years for joint research projects on immunoinflammation
	June 2008	QB3 Institute	$9.5 million for projects that will speed translation of discoveries to drugs

Institutional disagreements

Clinical research is not the only area where company funding presents conflicts. Companies are increasingly turning to academic sources to bolster their pipelines. In the past year alone, three major deals have been signed: GlaxoSmithKline of Brentford, UK, partnered with the Boston-based Immune Disease Institute to develop immunoinflammatory drugs; AstraZeneca of London will develop novel diabetes and obesity drugs in a deal with New York's Columbia University Medical Center; and Pfizer of New York is pursuing a variety of therapeutic areas with the California Institute for Qualitative Biosciences (QB3), a consortium of researchers from UCSF, the University of California, Santa Cruz, and the University of California, Berkeley.

The Pfizer-QB3 deal is part of a larger experiment at Pfizer to pursue a small-biotech model of drug discovery. It relies on a 'matchmaking service' that polls prospective Pfizer researchers looking to collaborate and then identifies QB3 researchers with similar interests. The impetus for collaboration can also stem from QB3 researchers. To encourage faculty participation, QB3 put out a call for proposals that generated such an enthusiastic response that the resulting applications nearly overwhelmed the review system.

To speed the process, Pfizer has developed master agreements that can be quickly drawn up and tailored to a specific research project. The company took inspiration from the high-tech industry. "Companies like Intel have been doing these kinds of agreements with places like Berkeley and Stanford for years," says Corey Goodman, who is president of Pfizer's Biotherapeutics and Bioinnovation Center, which inked the deal with QB3.

Regis Kelly, a professor of biochemistry and biophysics at UCSF and QB3's director, outlines some key concerns that QB3 addressed in its negotiations with Pfizer. Academic officials wanted to ensure that Pfizer would not control the publication of research. The agreement gives Pfizer six weeks to preview a draft of a paper before it is published so that the company can determine whether it wants to patent results. The Pfizer agreements call for research milestones, which can be a sticking point for some academic scientists who are used to more open-ended research. To help faculty, UCSF has put together a project-management program designed to assist faculty in developing appropriate milestones and timelines.

Of course, Pfizer also gets an IP benefit from the arrangements. The company gets the first negotiation rights for any IP that emerges. "We warn faculty that if they think they might want to start their own company, we recommend they do not apply for Pfizer funding," says Kelly. One advantage to the Pfizer-QB3 agreement is that participation is entirely voluntary. "Nobody has to do this. There is no compulsion to take any of this money."

Going forward

The public backlash against academia-industry partnerships has led some to reconsider the way they do business with each other. "Each side has to give up some prejudices and lines [it has drawn] in the sand. Academia has to get a little more reasonable about its financial expectations from its licensed intellectual property, and pharma has to be a little more reasonable in our understanding that they are going to want to publish and talk about their exciting research results at meetings," Goodman says.

In fact, many of the problems may stem from a lack of consistent practice and oversight. Industry and academic scientists may have broadly similar goals, but a rushed process can lead to problems and misunderstandings. "The problem comes when contracts don't go through the normal vetting process," says Cho.

Medical centers are also becoming more transparent in their disclosure of research funding from industry, partly in response to reports that institutions haven't been reporting potential conflicts and partly in anticipation of legislation that may require it. "They're seeing the writing on the wall," says Cho.

Institutions are trending to stricter policies, Lee says, in part because they don't want negative publicity from real or perceived conflicts of interest. Still, individual university policies range from disclosure of industry ties to the university (for example, at the University of Texas Medical Branch at Galveston) to mandates to disclose such relationships to the public under some circumstances (for example, at Washington University School of Medicine in St. Louis). Disclosure may also apply only to certain individuals, such as those who serve on purchasing committees and those with financial ties to industry (for example, at Mount Sinai School of Medicine in New York). Other academic institutions have no disclosure policies at all. The diversity of policies can lead companies to shop around. "Sometimes they'll hit up those institutions that have more lenient or lax policies," Lee says.

Washburn agrees: "It is very difficult for [university administrators] to act unilaterally, and it would be a lot easier if there were standards that all schools had to meet."

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Box 1 The pendulum swings at Harvard

Recently, a Harvard University committee took the unusual step of requiring instructors to disclose to classroom students any financial relationships that relate to the lecture topic. The announcement comes amid concerns about conflicts of interest as relationships between drug companies and universities continue to mount.

In addition, the university announced in February the formation of a new university-wide committee to review conflict of interest policies. The committee is tasked with updating Harvard Medical School's Conflict of Interest guideline, which was first adopted in 1990 and is typically updated every three to four years, according to Gretchen Brodnicki, dean for faculty and research integrity at Harvard Medical School. The last revisions were made in 2004. "[The committee was put together] in part because it was time, and in part because the landscape has changed quite a bit since 2004," says Brodnicki. For the first time, the committee includes student members.

Until now, the guidelines have focused entirely on research sponsorship, but gifts, sponsorship of education and other interactions have come under fire in recent years, prompting the committee to expand its purview into these areas.

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Economic pressures on the biotech industry could exacerbate the problem. Faculty interested in starting their own companies may find it difficult to find venture capital money, leading them instead to partner with existing biotech companies. "It potentially could shift the balance of power towards the companies. If there is a limited supply of partners, it gives the biotech companies much more power in stipulating the nature of the relationship," says Campbell. What's more, the potential for relationships to go awry may also increase as established biotech companies (rather than big pharma) that are more accustomed to striking licensing deals and negotiating with startups rather than with universities begin collaborating directly with academics. Such companies do not have the internal expertise about industry-academia liaison that big pharma companies have, and they may not have adequate knowledge of all the competing interest issues that can arise when working with an academic partner.

This landscape can be difficult for academic researchers to navigate. One organization hopes to improve the situation through professional education. Arbor Vitae (London) was founded when Peter Aitken, who was R and D director of the social service agency Devon Partnership Trust of Exeter, realized that few physicians receive instruction in how to manage relationships with companies and avoid conflicts of interest. "We noticed that there was very little peer discussion about working with industry. When we pulled people together, it was often the first time they had [talked about] it," says Aitken, who continues his work with Devon, while serving as Arbor Vitae's medical director. Arbor Vitae set up a series of training workshops to help physicians better understand companies and their motivations. Aitken wants to educate physicians about the culture of pharmaceutical companies and their research priorities, including "the awareness of strategic marketing from the first human dose. You can't escape marketing."

Educational initiatives are useful, but others have suggested more fundamental changes to the system. More government funding for translational research would pay big dividends, says Stephen Buxser, a research analyst at the industry research firm Nerac of Tolland, Connecticut. "[Governments] should fund them and not criticize them when it doesn't turn into a drug next week. There are a lot of ideas that with more time and money could be turned into good drugs. [During development], you're going to run into all kinds of biological barriers, and if you don't have the time to work around them, you're not going to end up with much at the far end. We are lacking a step in there, and that's enough money for translational research," Buxser says.

Others see ways to fine tune the relationships between academia and industry. One model would have universities accept money from industry and put it into a collective fund. Investigators could then apply for grants from the fund, thus removing any direct link to industry. It's a model that could be effective, Lee says, but it has at least one important disadvantage for industry: there is no guarantee that the academicians they favor will perform the research—a major disincentive. "They need to advance their mission," Lee concedes.

In fact, no one denies the importance of the private sector in the commercial development of academic discoveries. "Industry is going to continue to fund research because the government doesn't have enough money to do it. Industry should be at the forefront of doing applied drug studies because that is where they make their money. It's perfectly legitimate," says Sheldon Krimsky, author of *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* and an adjunct professor of public health and family medicine at the Tufts School of Medicine in Boston. But he argues that it is in industry's own interest to allow dissenting opinions to be published by their academic colleagues and collaborators. "It's very costly for industry, both in terms of dollar costs as well as their image, if they don't follow the highest standards of scientific integrity. If someone publishes an article that doesn't say what they want, that person shouldn't be blackballed. If it's good science, [companies] should be pleased that they learned earlier rather than later that something could be hazardous," he says.

According to Krimsky, an absence of academic freedom would eventually undermine the entire industry. "It will be a lot like the financial industry. Eventually it will catch up to somebody and the whole thing will collapse," he says

Blumenthal points to his research showing that academic scientists with high levels of industry funding publish less than scientists with moderate amounts of funding. "I think universities that aspire to be great universities should look very carefully at faculty members who consistently get all their funding from industry. They should ask themselves whether that scientist is capable of competing with peers for federal funding, which is a marker of success. Those things should be considered in the promotion process," says Blumenthal.

Given the fiscal realities of research funding, university-industry partnerships are undoubtedly here to stay, and research suggests there are plenty of positive impacts from industry funding. "It's tough because we have to receive funding, and the pot of money from National Institutes of Health and other sources is dwindling. So we apply to private foundations and to industry. A purist would say that all funding should come from government, but the reality is you have a portfolio," says Lee.

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