

WHEN ROBERT LINDSAY CHOSE TO BECOME A medical researcher in the early 1970s, he did not do it for the money. His field—the effect of hormones on bone—was a backwater. It was also a perfect opportunity for a young researcher to make his mark and, he hoped, help millions of people who suffered from the bone disease osteoporosis. As the body ages, sometimes bones lose the ability to rebuild themselves fast enough to keep pace with the normal process of

IS DRUG RESEARCH TRUSTWORTHY?

The pharmaceutical industry funnels money to prominent scientists who are doing research that affects its products—and nobody can stop it

By Charles Seife

deterioration, and the skeleton weakens. Neither Lindsay nor anyone else understood much about why this happened, but there was reason to think that hormones might play a role. Some women develop osteoporosis shortly after menopause, when their hormone levels drop sharply, perhaps upsetting that balance between bone creation and destruction. If so, Lindsay reasoned, replacing the hormones with a pill might halt or even reverse the progress of the disease. From a tiny, underfunded clinic in Glasgow, Scotland, he set up one of the first clinical trials of estrogen replacement therapy for bone loss in postmenopausal women. Lindsay's star was rising.

His next project had big commercial implications and got the attention of the drug industry. Having moved to Helen Hayes Hospital, a rehabilitation center north of New York City, in 1984 he published work that established the minimum effective dosage of an antiosteoporosis estrogen drug called Premarin. Because the findings suggested that fighting osteoporosis was tantamount to encouraging millions of women to use the drug, it made Lindsay an important person in the eyes of the drug's manufacturer, Wyeth-Ayerst Laboratories. Indeed, the company gave him a role as an author of its informational video *Osteoporosis: A Preventable Tragedy*.

By the mid-1990s, when Wyeth got caught in a patent battle over Premarin, Lindsay was a staunch Wyeth ally. He came out against approval of a generic version of the drug that would have cut into sales even though the generic form would have made it easier for osteoporosis patients to receive therapy. His reasoning was that such versions might not be precisely equivalent to the brand-name drug, a fact that can be true with certain drugs but was also a position that happened to echo the company line. "All we're asking is that we don't approve something now and regret it" later, he told the Associated Press in 1995. Lindsay's close relationship with Wyeth and other drug companies carried on for decades, in ways that were sometimes hidden. He started allowing Wyeth to draft research articles and began taking tens of thousands of dollars from pharmaceutical interests that stood to gain from his research.

The scandal is not what Lindsay did so much as that his case is typical. In the past few years the pharmaceutical industry has come up with many ways to funnel large sums of money—enough sometimes to put a child through college—into the pockets of independent medical researchers who are doing work that bears, directly or indirectly, on the drugs these firms are making and marketing. The problem is not just with the drug companies and the researchers but with the whole system—the granting institutions, the research labs, the journals, the professional societies, and so forth. No one is providing the checks and balances necessary to avoid conflicts. Instead organizations seem to shift responsibility from one to the other, leaving gaps in enforcement that researchers and drug companies navigate with ease, and then shroud their deliberations in secrecy.

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"There isn't a single sector of academic medicine, academic research or medical education in which industry relationships are not a ubiquitous factor," says sociologist Eric Campbell, a professor of medicine at Harvard Medical School. Those relationships are not all bad. After all, without the help of the pharmaceutical industry, medical researchers would not be able to turn their ideas into new drugs. Yet at the same time, Campbell argues, some of these liaisons co-opt scientists into helping sell pharmaceuticals rather than generating new knowledge.

The entanglements between researchers and pharmaceutical companies take many forms. There are speakers bureaus: a drug-maker gives a researcher money to travel—often first class—to gigs around the country, where the researcher sometimes gives a company-written speech and presents company-drafted slides. There is ghostwriting: a pharmaceutical manufacturer has an article drafted and pays a scientist (the "guest author") an honorarium to put his or her name on it and submit it to a peer-reviewed journal. And then there is consulting: a company hires a researcher to render advice. Researchers "think what these companies are after are their brains, but they're really after the brand," says Marcia Angell, former editor in chief of the *New England Journal of Medicine*. "To buy a distinguished, senior academic researcher, the kind of person who speaks at meetings, who writes textbooks, who writes journal articles—that's worth 100,000 salespeople."

Peer-reviewed journals are littered with studies showing how drug industry money is subtly undermining scientific objectivity. A 2009 study in *Cancer* showed that participants somehow survived longer when a study's authors had conflicts of interest than when the authors were clean. A 1998 study in the *New England Journal of Medicine* found a "strong association" between researchers' conclusions about the safety of calcium channel blockers, a class of drugs used to reduce blood pressure, and their financial relationships with the firms producing the drugs.

It is not just an academic problem. Drugs are approved or rejected based on supposedly independent research. When a pill does not work as advertised and is withdrawn from the market or relabeled as dangerous, there is often a trail of biased research and cash to scientists. For example, in the mid-2000s, when patients started suing Wyeth about another estrogen drug, Prempro (which has been linked to the risk of breast cancer, strokes and certain other diseases), Wyeth's ghostwriting/

IN BRIEF

Many researchers maintain close financial ties to the drug companies that stand to gain from the results of their research.
Congress passed the Physician Payments Sunshine

Act, which, starting in 2013, will compel pharmaceutical firms and medical device manufacturers to reveal most of the money that they are putting into the pockets of physicians.

Yet as the case study in this article shows, neither scientific institutions nor the scientists themselves have shown a willingness to police conflicts of interest in research.

guest-authorship arrangements became a central part of the case. When it was the turn of Merck's Vioxx painkiller (which was linked to heart attacks and strokes), drug industry money came up, too. In one Vioxx study, for example, academic researchers appear to have signed on to a Merck-sponsored project after the company had already done all the data analysis. According to a 2010 study that appeared in the *British Medical Journal*, 87 percent of researchers who expressed "favorable views" of GlaxoSmithKline's diabetes drug Avandia, despite indications that it might increase the risk of heart attacks, had some financial involvement with the drug's manufacturer. And when a U.S. Food and Drug Administration committee debated whether or not to pull Avandia from the market because of the link to heart attacks, it came out that members of the committee, too, had been taking money from drug companies.

The scientific community's answer to the conflict-of-interest problem is transparency. Journals, grant-making institutions and professional organizations press researchers to openly declare—to their research subjects, their colleagues and anyone else affected by their work—when they have any entanglements that might compromise their objectivity. That way the scientific community decides whether a study is ethical and, when the experiment is done, how far to trust the results. It is an honor system. Researchers often fail to report conflicts of interest—sometimes because they do not even realize that they present a problem. (*Scientific American* also asks for voluntary disclosures about conflicts from researchers who write articles.)

In theory, there is a backup system. Several layers of checking are supposed to ensure that conflicts of interest are caught and exposed even when an oblivious or dishonest researcher does not report them. When a scientist fails to report such a conflict, the university or hospital he or she works for is supposed to spot it and report it. And when a university or hospital is not doing its job catching conflicted research, then the government agency that funds most of that research—the National Institutes of Health—is supposed to step in. Unfortunately, that backup system is badly broken. "Institutions often look the other way, or they have policies in place that are quite weak," says Adriane Fugh-Berman, a professor in Georgetown University's department of pharmacology and physiology. More shockingly, the NIH is not only failing to enforce ethics laws intended to stop the creeping influence of drug company money, but it may also be breaking those laws.

Congress has been trying to stop corruption of medical research through legislation. In 2010, as part of the health care reform package, it passed the Physician Payments Sunshine Act. Starting in 2013, the law compels all pharmaceutical companies and medical device manufacturers to reveal most of the money that they are putting in the pockets of physicians. Because most (but not all) medical researchers are medical doctors, in theory, these data will help universities, research hospitals and the NIH to pin down whether a grantee has a potential conflict of interest. The information, however, will be worthless unless it is used.

The case of Robert Lindsay shows how deep the problem of conflicted medical research is and how difficult it will be to fix.

A THICKET OF ENTANGLEMENTS

THE EFFORT OF PHARMACEUTICAL COMPANIES to influence science discourse often takes the form of ghostwriting. Once a drugmaker can steer the way that a research article is written, it is able to

control, to a large degree, how a scientific result is understood and used by clinicians and researchers.

One of Lindsay's most prestigious papers—a 2002 article demonstrating Prempro's beneficial effects on postmenopausal women—was initially drafted by DesignWrite, a firm that had been hired by Wyeth to ghostwrite articles for publication in the peer-reviewed literature. After meeting with Lindsay in mid-April 2001 to discuss developing the paper, DesignWrite then created an outline and forwarded it to Lindsay (and Wyeth). DesignWrite sent a draft to Lindsay for comments by early June, did some additional analysis and revised the manuscript. In August the *Journal of the American Medical Association* accepted it for publication. Later in the year DesignWrite revised the manuscript in response to comments, and the paper was published in May 2002. At the end of the article, Lindsay and his three co-authors thanked Karen Mittleman for her editorial assistance without identifying her as an employee of DesignWrite or disclosing its relationship with Wyeth.

Lindsay denies that DesignWrite had a large role in shaping the 2002 paper or any of his subsequent ones. Rather the firm would merely "provide a draft under our direction," he says. He and the other named co-authors were responsible for the design and direction of the study. If so, Lindsay deserves to be listed as a co-author of the paper, and Mittleman does not deserve anything more than the brief acknowledgment, according to Phil B. Fontanarosa, executive editor at *JAMA*. "It is not apparent that [Mittleman's] activities included conception and design (of the study), acquisition of data, or analysis and interpretation of data," he wrote in an e-mail to me.

This use of an outside writing firm was not a one-shot deal. Kathleen Ohleth, then a writer for DesignWrite, helped Lindsay draft a 2009 article for the journal *Fertility and Sterility*. (After my initial interview with Lindsay, he declined to answer any more questions, including those about who paid Ohleth in 2009, and referred me to a press officer.) Two years later, in an article in *Osteoporosis International*, Lindsay also thanked Ohleth for "medical writing support" and acknowledged that it was funded by Pfizer (which acquired Wyeth in 2009) but said that he "was the sole contributor to the concept and content direction of the paper." The article declared that a set of hormones in Pfizer's pipeline presented a "new paradigm for menopausal therapy."

At the same time that Lindsay was accepting writing support from Pfizer, he was accumulating a number of financial arrangements that posed a potential conflict of interest. According to a database compiled by the investigative journalism group ProPublica, in 2009 and 2010 Eli Lilly paid Lindsay more than \$124,000, much of it for speaking fees.

Most peer-reviewed journals have rules about disclosure of financial relationships. Precisely what a scientist has to disclose depends on the subject matter and on the journal, so it is hard to pin down exactly when a researcher is breaking those rules. In a number of publications, Lindsay did disclose his relationship with Lilly, but he did not do so uniformly. For example, in a September 2010 article in the *Mayo Clinic Proceedings* about an osteoporosis study, many of the authors declared that they were on Lilly's speakers bureau or had other entanglements with the company, although Lindsay, also a co-author, did not. He subsequently told me that he had changed his mind about declaring this kind of relationship: "Up until fairly recently, my declarations included any

pharmaceutical company whose products were in my talk” or article, he told me. “I’ve changed that philosophy a bit because now, to make sure that there’s real clarity, I would declare all contacts.”

Even when the subject of a study was a Lilly product, Lindsay did not always reveal his financial relationship with the firm. His 2008 study in the *Journal of Clinical Endocrinology and Metabolism* on whether teriparatide, the basis of Lilly’s drug Forteo, is affected by other osteoporosis drugs had no announcement that Lindsay had in recent years acted as a consultant and lecturer for Forteo’s maker. “Since everyone in that study was treated with teriparatide, there was no capability to create a conflict,” Lindsay says. “And, of course, [the study] wasn’t supported in any way by Eli Lilly.”

Lindsay’s inconsistent disclosure practice goes beyond research articles. As a prominent investigator, Lindsay has been instrumental in publishing guidelines that other physicians use to treat osteoporosis. For instance, he helped to develop and write the National Osteoporosis Foundation’s 2008 *Clinician’s Guide to Prevention and Treatment of Osteoporosis*. The guide, which has been endorsed by numerous physicians associations, talks about treatment choices, including teriparatide. (“Teriparatide is generally well tolerated, although some patients experience leg cramps and dizziness,” it says.) In a section marked “Disclosure,” the guide states that of the authors, including Lindsay, none of them has “a relevant financial relationship with any commercial interest.”

What is more, Lindsay apparently failed to mention these potential conflicts when applying for federal grants. Although he was a consultant for Lilly at least as far back as 2004, in 2005 he applied to the NIH, the agency in charge of most of the nation’s federally supported medical research, to fund a study of Forteo: Lindsay wished to biopsy patients’ bones to see how the drug was affecting their skeletal structure. He got the grant. Over the next few years the NIH gave Lindsay \$3.4 million to study the drug. In 2010 he applied for a new grant to compare two methods of administering Forteo. Again, he received the grant, this time for \$364,000, in 2010, and another, for \$346,000, in 2011.

Federal regulations about potential conflicts of interest in NIH grants stipulate that a grantee has to identify any real or apparent conflicts of interest and report how any such conflicts have been managed, reduced or eliminated. Failure to do so is a violation of the law. It seems clear enough, but in practice it is not at all clear. Responsibility for enforcement gets shifted from one institution to the other to such an extent that conflicts such as Lindsay’s often fall through the cracks.

FOLLOW THE CASH FLOW

THE NIH IS RESPONSIBLE for giving medical researchers tens of billions of dollars every year. With that much money at stake, there is tremendous potential for corruption. The NIH is not very good at stopping it because the agency is not aggressive about ferreting out conflicts of interest in its scientists’ work. When ap-

proached for this story about potential breaches of ethics rules, NIH officials closed ranks.

Asked about possible conflicts of interest in Lindsay’s grants to study teriparatide, Faye Chen, an NIH official, refused to provide copies of written assurances from Helen Hayes, Lindsay’s employer—paperwork required by federal law—that conflicts of interest had been properly dealt with. She insisted that everything was in order. “The NIH is committed to preserving the public’s trust that the research supported by the NIH is conducted without bias and with the highest scientific and ethical standards,” she wrote in an e-mail to me. She added, “I can assure you that Dr. Lindsay’s institution provided the required certification and assurance prior to receiving the award, and they will be required to provide this certification every year prior to award.” Documents

obtained through a Freedom of Information Act (FOIA) request contained no mention of any potential conflict of interest—nothing to indicate that Lindsay was taking money from the manufacturer of the drug being studied. NIH officials would not comment on whether or not they have followed up on the matter.

The NIH’s actions should come as no surprise. A few years ago the Department of Health and Human Services’s Office of Inspector General got its hands on internal NIH communications that show that management discourages investigations into conflicts of interest among NIH-sponsored researchers. (In the interest of transparency: my wife works for the Office of Inspector General but did not have anything to do with these studies or this article.) For example, one memorandum stated, “We should not follow up for additional details about the nature of the conflict or how it was managed unless there is sufficient programmatic concern to do so.”

Lindsay’s case does not appear to be an isolated one. Scientists around the country are

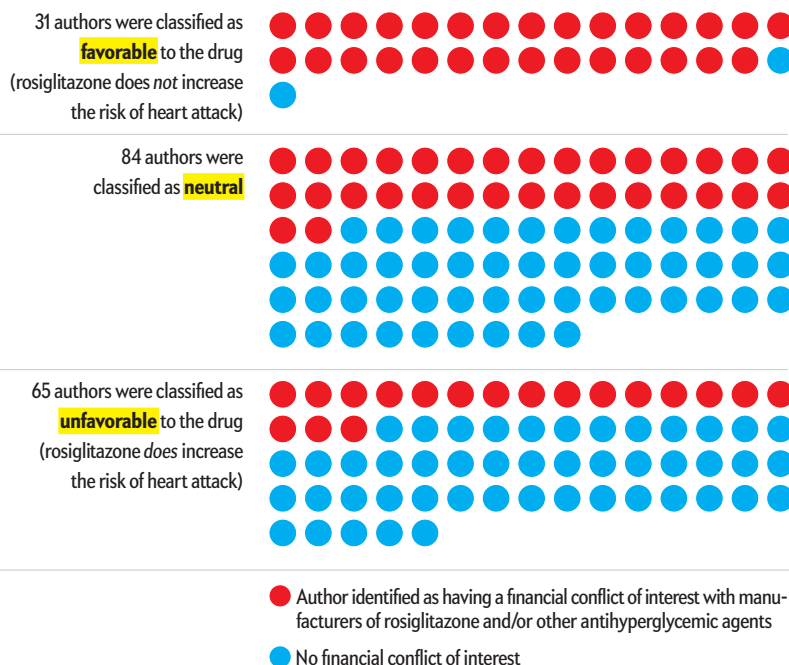
pursuing government-funded research at the same time that they are taking money from pharmaceutical companies, which often poses a potential conflict of interest. To get a sense of how much money is flowing from drug companies to NIH grantees, my students and I used a database that contains all NIH grants from 2009 and 2010 and used the ProPublica database of drug company payments to identify which ones were on a pharmaceutical manufacturer’s payroll. We were able to identify \$1.8 million in payments from a handful of drug companies to NIH grant recipients in New York State alone—payments for speakers bureau appearances, consulting jobs and other services. (The total payouts in New York are likely to be much higher.) Many of these payments might not pose actual conflicts of interest.

Grantees are not the only ones taking cash from drug companies—so are the people at the NIH who help to decide which researchers get the grants. Just as we used the ProPublica database to identify pharmaceutical industry payments to NIH-sponsored researchers, we used it to spot drug company money flowing to members of the NIH’s advisory and review committees. All told, we found nearly 70 advisory committee members taking a total of more than \$1 million for speakers bureau appearances, con-

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Case Study: Conflicting Interests

To what degree do financial entanglements influence the judgment of scientists? To find out, researchers at the Mayo Clinic in Rochester, Minn., focused on the diabetes drug rosiglitazone, which a meta-analysis had linked to increased risk of heart attacks. They examined articles that cited the meta-analysis or a subsequently released report on a large trial of rosiglitazone and found that scientists with a conflict of interest were more likely to view the drug favorably. “There was a clear and strong link between the orientation of authors’ expressed views on the rosiglitazone controversy and their financial conflicts of interest with pharmaceutical companies,” the report determined.



sulting and other services to the drug companies. Some of these payments may be violations of federal ethics rules, which prohibit advisory committee members from participating in decisions that might affect an organization from which they are receiving substantial remunerations.

The problem, then, goes much deeper than NIH grantees. Drug company money has seeped into the NIH itself. If the agency knew about its employees’ potential conflicts and failed to ensure that those conflicts did not affect their decisions on the committees, the agency itself is violating the law. To find out, I filed a Freedom of Information Act request for documentation that would indicate whether or not the NIH knew about drug company payments to its advisory committee members and, if so, whether it allowed the payees to perform their duties despite being on a pharmaceutical manufacturer’s payroll. The NIH refused to turn those documents over; I sued. After a nine-month-long lawsuit, a federal judge forced the NIH to release what it had tried to keep hidden.

Some of the documents revealed by the lawsuit imply that the NIH’s internal conflict-of-interest policing is largely devoted to finding missing forms. Further, they show that a number of NIH institutes appear to not have taken a single conflict-of-interest enforcement action against their employees since 2008. Yet the most revealing documents—ones that the NIH fought to keep hidden—have to do with what are known as waivers.

Under limited circumstances, the NIH can grant a waiver, which exempts a conflicted government employee (such as an advisory committee member) from ethics laws. I requested information about waivers that had been granted to several individuals sitting on NIH advisory committees, each of whom, I knew from the ProPublica database and other sources, had taken thousands of dollars from drug companies. I wanted to find out why the NIH was allowing these people to sit on committees despite a potential conflict—and, just as important, what the nature of those conflicts were.

The vast majority of the payments from drug companies were nowhere to be found in those waivers. For example, Louis Ptáček, who was then on the National Advisory Neurological Disorders and Stroke Council, was granted permission to take part in a number of meetings despite his numerous stock holdings in drug companies, but the waiver did not mention that he had received more than \$50,000 as a consultant for Pfizer. (Ptáček did not respond to a request for comment.) Similarly, a waiver for Arul Chinnaiyan, who sits on the National Cancer Institute’s Board of Scientific Advisors, did not indicate that he had received, from GlaxoSmithKline, \$9,000 in 2009 and \$21,000 in 2010. But Chinnaiyan said that he had disclosed these arrange-

ments with the NIH. Why, then, did they not appear on his waiver?

The NIH would not comment on individual cases. An NIH official agreed to speak on general policy but only under the condition that she not be named. Consulting fees and speakers bureau arrangements, she said, generally would not be listed on a waiver but instead on a separate document that deals with specific issues about which committee members must recuse themselves. As this article went to press, Susan Cornell, a FOIA officer at NIH, confirmed that the agency had failed to hand over certain recusal documents in response to my FOIA request, as it was supposed to do.

The NIH’s inconsistent disclosure of documents and the secrecy behind them make it impossible to say with absolute certainty what is going on. At the very least, the NIH is doing a sloppy job of policing potential conflicts. For example, if consulting arrangements belong on a recusal document, why do Lawrence R. Stanberry’s consulting arrangements with GlaxoSmithKline and Starpharma appear on his waiver? (Stanberry, chair of the pediatrics department at Columbia University’s College of Physicians and Surgeons, sits on the National Institute of Allergy and Infectious

SOURCE: “ASSOCIATION BETWEEN INDUSTRY AFFILIATION AND POSITION ON CARDIOVASCULAR RISK WITH ROSIGLITAZONE: CROSS-SECTIONAL SYSTEMATIC REVIEW” BY AANYI T. WANG, CHRISTOPHER P. MCCOY, MOHAMMAD HASSAN KURAD, AND VICTOR M. MONTORI, IN *JAMA*, VOL. 340, NO. 750; APRIL 10, 2010

Diseases's Board of Scientific Counselors.) And why does the waiver not include the consulting work he has done for Sanofi Pasteur? "I don't know why the consulting at Sanofi did not appear to be on the waiver," Stanberry wrote to me in an e-mail. Perhaps the officers in charge of producing waivers made mistakes.

THE ENFORCEMENT SHELL GAME

INFORMATION obtained by another Freedom of Information Act request—this time to the Office of Government Ethics (OGE), the agency that is in charge of ensuring that government agencies such as the NIH are following ethics rules—implies that the NIH is not complying with federal regulations about waivers.

From the government's point of view, granting a waiver is a serious matter; it is essentially granting immunity from a law, and it is supposed to be done only rarely and with a good deal of oversight. Federal regulations dictate that the NIH must check in with the OGE before making such grants. The NIH has issued dozens of such waivers for advisory committee members in recent years, but since 2005 the ethics office had documented only three times where the NIH consulted with the office as required, and none of the waivers in question had to do with a member of an advisory committee. When I asked NIH officials about this issue, they insisted that the agency was fully in compliance with federal regulations when it comes to issuing waivers but did not provide any evidence that the NIH was consulting with the OGE when issuing waivers as required by law.

The institutions that administer grants are supposed to provide another check on conflict of interest, but they do not. Historically, the NIH has not taken responsibility for policing conflicts of interest in the research it funds. In 2007, responding to the Office of Inspector General's complaint that the NIH's handling of financial conflicts of interest was woefully inadequate, Elias Zerhouni, then director of the agency, maintained that it was not the NIH's job to figure out whether its grantees were obeying ethics laws. "We believe it is vital to maintain objectivity in research," he wrote in a letter to the Office of Inspector General, "however, responsibilities for identifying ... FCOIs [financial conflicts of interest] must remain with grantee institutions." NIH officials say that current policy on the matter has not changed.

Yet grantee institutions also have a record of failing to address ethical issues involving their researchers. A 2009 report by the Office of Inspector General looked at how organizations that receive NIH grants find potential conflicts of interest. Ninety percent of them left it up to the researcher's discretion to identify any problems. Even institutions that publicly take a hard line against conflicts of interest are often lax in enforcing their policies. In late 2010 ProPublica developed a drug company database and started checking up on Stanford University and several other universities with strong anti-conflict-of-interest policies. They found dozens of faculty members who were taking pharmaceutical money in violation of those institutions' rules.

Helen Hayes, where Lindsay works, does not seem to rigorously enforce its own rules. To be sure, the organization is complex—it is a state facility, so the New York State Department of Health has an interest, and all its grants are administered through Health Research, Inc. (HRI), a nonprofit organization that helps the state health department get external funding for medical research. HRI administers half a billion dollars a year in grants. With so many grants and so much money at stake, however, it is surprising that HRI is not identifying scores of conflict-of-interest cases every year. "I've been director of sponsored programs here for 11 years, and I've been employed by Health Research doing grant administration for 17 years. I've never seen a conflict of interest," Terry Dehm of HRI told

me. "Not a single conflict of interest on any grant that we've applied for... We've just never seen it."

When I told her that Lindsay's NIH grant to study Forteo, which was administered by HRI, draws income from the manufacturer of the drug he is using federal funds to study, Dehm said that HRI's then executive director, Michael Nazarko, would call that afternoon or the next day. He never did so, nor did he respond to repeated attempts to follow up. Through a New York State Department of Health press officer, Nazarko eventually declined to answer any questions, as did Val Gray, the CEO of Helen Hayes. Felicia Cosman, Helen Hayes's clinical research director, also declined. Cosman took NIH money to study Forteo even though Lilly paid her more than \$135,000 for speaking and consulting, according to ProPublica. When asked for comment, Helen Hayes and HRI e-mailed a copy of their conflict-of-interest policies and a statement that insisted that "the procedures outlined in this policy have been followed" with Lindsay's and Cosman's grants.

A few days after I called Helen Hayes to inquire about Lindsay's work and potential conflicts of interest, hospital officials called for an ethics review of that work. Initially, the hospital sought to find an independent panel to review whether or not Lindsay's work was conflicted because of his relationship with Lilly. Failing to find an independent panel, however, the hospital asked the Helen Hayes Hospital Institutional Review Board (IRB) to take a look. (Lindsay was then a member of the board, but he sat out of the deliberations.) The board found that Lindsay had taken significant payments from Lilly but that the payments did not pose a conflict of interest. I found out about these proceedings months later, after using New York State's Freedom of Information Law for documents related to the grants.

Unfortunately, an IRB—which is set up to approve research protocols in a clinical trial and ensures that patients are treated properly—is ill equipped for answering questions about financial conflicts of interest. "The composition of an IRB was never designed to handle [conflict of interest] in today's world," notes Arthur Caplan, a bioethicist at New York University Langone Medical Center (and a member of the board of advisers for *Scientific American*). "It's pretty clear to me that this guy at Helen

Researchers cannot stop the influence of drug company money. Hospitals and universities will not do it. The NIH will not do it. As a result, millions of taxpayer dollars fund research whose objectivity is being undermined.

Hayes has a pretty serious conflict,” Caplan says. Carl Elliott, a bioethicist at the University of Minnesota, agrees. “The IRB was the wrong body to ask for an opinion,” he told me in an e-mail.

In any case, Helen Hayes is not geared to rooting out conflicts. Lawyers there adapted the boilerplate language from NIH grant guidelines requiring that a researcher report, among other things, “anything of monetary value, in cash or in kind, *from a research sponsor* (e.g., consulting fees, honoraria, or travel, meals or entertainment).” (Italics added for emphasis.) The inserted clause narrows the scope of what needs to be disclosed. Because Lilly is not the sponsor of Lindsay’s research—the NIH is—payments from Lilly would not seem to be a conflict of interest under these guidelines. Indeed, it is difficult to conjure a circumstance in which an NIH grantee would have a conflict of interest under Helen Hayes’s rules. There is no reason to think that Helen Hayes is special in this regard. Institutions that administer grants have no real incentive to worry about conflicts. The more grant money their employees get, the better for the employer. Why kick up a fuss?

FIXING THE SYSTEM

RESEARCHERS cannot stop the influence of drug company money. Hospitals and universities will not do it. The NIH refuses to do it. And as a result, millions of taxpayer dollars fund research whose objectivity is being undermined. Congress, which holds the purse strings, is hopping mad.

Most of its wrath is directed at the NIH, which it has called to task for not following ethics guidelines. “I am well acquainted, from my years as chairman of this subcommittee, with the attitude often found at the NIH: the rules don’t apply to us,” said Representative Joe Barton of Texas, then chair of the House Energy and Commerce Committee, at a hearing in 2004 about ethical lapses at the NIH. “One can only wonder: if the NIH can be so permissive about the most basic ethical rules in the federal government, what does this say about the NIH’s ability to manage taxpayer dollars and, most important, ensure that taxpayer-supported research gets translated into cures?” he added. Yet the attitude persists even after Congress has put increasing pressure on the NIH to mend its ways.

Starting in 2008, Senator Charles Grassley of Iowa led a set of congressional inquiries into several incidents in which NIH grantees failed to reveal payments from drug companies and universities failed to discipline the researchers involved properly. The most prominent example was the case of Charles Nemeroff, who, until recently, was chair of Emory University’s psychiatry department. Emory documents showed that as early as 2000, there were questions about the propriety of Nemeroff’s ties to industry—such as money he was taking from drugmaker Smith-Kline Beecham, which later became GlaxoSmithKline. (The company also had donated money to endow a chair in Nemeroff’s department.) In 2003 researchers accused Nemeroff of not disclosing his ties to the manufacturers of three treatments covered in a *Nature Neuroscience* article. (*Scientific American* is part of Nature Publishing Group.)

Emory’s response was to hold an investigation. In 2004 the university determined that Nemeroff had, in fact, committed “many violations of the Conflict of Interest, Consulting, and other policies.” Confronted with these findings, Nemeroff agreed to limit his consulting with GlaxoSmithKline because of the impli-

cations it might have for an NIH grant he was working on, as well as to reduce his involvement with various other firms. After a congressional inquiry in 2008 revealed numerous undisclosed payments, Nemeroff stepped down as chair of Emory’s psychiatry department, and Emory prohibited him from applying for NIH-sponsored grants for two years. Nemeroff has since left Emory for the University of Miami, where he is now chair of the department of psychiatry and behavioral sciences and the principal investigator on a new \$400,000 NIH grant.

After these congressional inquiries, the NIH adopted revised regulations that require grantees to disclose all financial entanglements greater than \$5,000 to their home institutions. In addition, the rules compel those institutions to make a public accounting, in broad terms, of any conflicts of interest of personnel involved in NIH-sponsored research. These changes mean that the public will have access to more information about the targets of pharmaceutical industry money.

NIH director Francis Collins trumpeted the new regulations as “a clear message that the NIH is committed to promoting objectivity in the research it funds.” Yet there was no language in the new regulation that changed who is responsible for spotting such conflicts or how ethical problems are managed. “Because the institutions themselves know the context in which their employees work and because these are employees of the institution and not employees of the federal government, the management responsibility resides with them,” says Sally Rockey, the NIH’s deputy director for extramural research. “The institutions are in the best position to manage the financial interests of their own employees.”

The only hope of solving the problem of conflicted science rests with the researchers themselves. The culture of science can change. Through the agency of peer-reviewed journals (whose reputations suffer as a result of biased research) and via learned societies (which set the ethical standards that scientists are supposed to abide by), scientists can exert pressure on their peers to forgo drug company money. At the very least, they might convince their fellow scientists that it is in their long-term interest to be completely open about the payments they are taking from pharmaceutical firms.

The best hope to provide ethical guidance and to exert peer pressure lies in the professional organizations and peer-reviewed journals. In Lindsay’s field, those would be the National Osteoporosis Foundation and *Osteoporosis International*. Would these organizations be willing and able to take the lead in rooting out conflicts of interest? One person to ask might be the former president of the National Osteoporosis Foundation and the current editor in chief of *Osteoporosis International*—Robert Lindsay. ■

MORE TO EXPLORE

ProPublica database cited in this article: <http://projects.propublica.org/doccdollars>
University of California, San Francisco, database of drug-industry documents: <http://dida.library.ucsf.edu>
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Links to the documents and studies that Seife used to research this article are available at ScientificAmerican.com/dec2012/drug-research