From NATIONAL PUBLIC RADIO – Medical Malpractice by the Pharmaceutical Industry Researchers?

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BROOKE GLADSTONE: Last month, a panel convened by the National Institutes of health recommended new levels for cholesterol so low that many more Americans would have to take expensive drugs to meet them. Then we learned that most of the members of that panel had ties to drug companies that made those expensive drugs. That was merely the latest example of conflict of interest in medical research that has put watchdog groups and some lawmakers on edge. Huge institutions and top flight universities often are tainted by the corporate money that funds their research, but that's okay, because we have medical journals, those peer-reviewed paragons of probity, to sniff out the real breakthroughs buried in all of those steaming piles of hype. Our doctors rely on those journals, and we rely on our doctors. But according to the research institute we call Bob Garfield, probably we trust too much.

BOB GARFIELD: No, you certainly can't blame Congressman Peter Deutsch for diagnosing the NIH with the, quote, "disease of greed." And you can't but be appalled when universities, our cathedrals of higher learning, ride on the same gravy train. And when you sit in the internist's office, waiting for the doctor to appear, and you scan the array of Lipitor notepads and Viagra ballpoint pens, you can scarcely help wondering about what, exactly, it takes to influence what drugs get prescribed. But while you're scanning, you might also take a long, hard look at those neat stacks of handsomely bound medical journals, because within them are research studies, review articles and editorials whose findings are as susceptible to the greed disease as any other part of the system.

RICHARD SMITH: I sometimes find myself worrying that a lot of medical journals have become almost a marketing arm of the pharmaceutical industry.

BOB GARFIELD: Richard Smith is the editor in chief of the venerable British Medical Journal.

RICHARD SMITH: For the New England Journal of Medicine, Lancet and JAMA, about 70 percent of the randomized trials they publish are funded by the pharmaceutical industry. Now, that gets to be increasingly bothersome when you realize how good the pharmaceutical industry is at getting the results they want.

BOB GARFIELD: Consider, to begin with, the journals' standard practice of permitting scientific authors with financial ties to manufacturers to publish on the very drugs those manufacturers produce, the rationale being that otherwise the journals would have no access to the most distinguished researchers in their fields. Dr. Jeffrey Drazen is the editor of the New England Journal of Medicine.

If we're going to have new pharmaceuticals, they're developed by commercial entities. There needs to be an interface between the people who evaluate those drugs and people who make the drugs. If we didn't have such an interface, we'd still be using leeches.

BOB GARFIELD: Yes, it is axiomatic that science's greatest advancements are fueled, one way or another, by self-interest, and obviously somebody must review and chronicle the results. The problem arises when those processes are influenced by another familiar axiom, "He who pays the piper calls the tune." Shannon Brownlee, journalist and fellow with the New America foundation, has painstakingly documented industry efforts to put drugs in the best possible light, and these, she says, are message management techniques that even the most gimlet-eyed peer reviewer is often incapable of detecting.

Peer review can only do so much, and one of the things that peer review cannot do is it cannot know which part of the data you're not even presenting. It cannot know what negative findings aren't even being submitted to the journal. And that's one of the big problems here: we don't really know how much negative data are out there.

BOB GARFIELD: There is a growing clamor for all clinical trials to be registered, irrespective of results, as more evidence surfaces that pharma companies routinely quash results that don't come out just right. Dr. Jane Garland heads the Mood and Anxiety Disorders Clinic at Children's and Women's Hospital in Vancouver, British Columbia. In 2001, GlaxoSmithKline enrolled some of her patients in a study on the use of the antidepressant Paxil on children. As part of the standard legal paperwork with the manufacturer, Garland agreed to keep all records pertaining to the study, including summaries of previous trials, strictly confidential for 10 years.

JANE GARLAND: That was fine, until I read the Paxil literature that they gave me, which included the results or just a summary of the results of two previous negative trials in depression, and my jaw dropped. Oh, my goodness, why didn't I know this? Why wasn't this information available to me? And I began to wonder: Who else knows this?

BOB GARFIELD: Garland decided to go public in a paper that cited the incidence of unpublished trials and warned fellow researchers not to be tricked or co-opted by enforced silence. She showed a draft to an American colleague.

JANE GARLAND: He said the paper was well-written, the results were cogent, but not to write anything about it, because I will do tremendous disservice to children, because we know these medications work. And I'm sort of scratching my head, saying well, how do we know the medications work when the data's piling up on the side of not very much evidence that they work? And in fact, when all the data came out, 12 out of 15 antidepressant studies were negative in kids.

BOB GARFIELD: The most alarming of the previously suppressed news: a correlation between adolescent use of antidepressants and suicide. Far from warning the public, GlaxoSmithKline simply enrolled new groups of test subjects on the chance that the results would improve.

JANE GARLAND: So, to use an example, if you roll a die, you know, there's a chance it could come up anything from 1 to 6. What if you roll the dice, and every time you get something other than a 6, you don't write it down. And that's essentially what's happened.

BOB GARFIELD: In June, a few days after the State of New York sued over this issue, GlaxoSmithKline issued a press release calling its disclosure policy "accepted standard practice for making data available." One week later, though, the company announced a forthcoming website that will summarize results of all of its clinical trials. It's naturally frustrating for companies who spend billions to develop drugs only to have the dice-throw of medical research return not big fat 6's but lots of 2's and 3's. That's when it's especially helpful to have in your employ authors paid to be not overly pre-occupied with the 2's and 3's. Last year, London Observer reporter Antony Barnett looked into an article in the Journal of Alimentary Pharmacology about the side-effects of ulcer treatments.

ANTONY BARNETT: There are a number of top-notch academics listed at the top of the paper, but we found out the paper was actually written by a medical writer working for AstraZeneca, which is a large British drug company that was promoting one of the drugs in the study, and lo and behold it came out to find out that the side-effects listed for that particular drug were less than had previously been reviewed.

BOB GARFIELD: The practice is called medical ghostwriting, which sometimes is a benign aid to brilliant scientists whose brilliance doesn't extend to their prose, and sometimes, according to Shannon Brownlee, an elaborate apparatus for laundering results.

What happens is a pharmaceutical company will fund a study which may be done in-house, may be done by doctors in community practice, which may be done by academic clinicians, it's -- or some combination. So the companies go out, and they hire this PhD, and the PhD writes up the paper with just the right interpretation of the data, and then the medical communications company goes and finds what's known in the business as a KOL --and the KOL is a Key Opinion Leader -- an academic clinician who's a big noise in their field. And they approach this person, and they say: We have this paper. We know you're a terribly busy person. And would you like to author this paper, which we happen to have already written?

BOB GARFIELD: Though that authorship is not likely to be apparent to anybody. Antony Barnett interviewed a ghostwriting agency researcher named Susanna Rees who told him her job was to handle floppy disks going in the mail to journal editors and to electronically cover the trail.

ANTONY BARNETT: And one of her particular jobs was to go through the computer history on the disk to ensure that there was no way of telling that the original research had come from a drug company or that the original author was a ghostwriter.

BOB GARFIELD: The New England Journal's Jeffrey Drazen himself encountered this process when he emailed a listed author on a bit of research data and got a return call not from the author, but from a drug company employee.

He called me up and got on the phone and he said: What exactly do you want to know? And I thought about it for a while, and I said: I think I know everything I need to know.

BOB GARFIELD: Drazen insists safeguards are in place, at least at his publication, to ensure that listed authors are genuine authors and that pertinent conflicts are disclosed. But what is never disclosed is a more insidious motivation still: the journal's own dependence on drug company revenue. A February story in the Washington Post documented a case at the Journal of Dialysis and Transplantation in which the publication's marketing department vetoed an article unfavorable to one of its key advertisers, the biotech firm Amgen. And there's more. In addition to advertising, medical publishers reap enormous revenues from drug marketers for reprint rights to journal articles -- positive ones only, of course. The British Medical Journal's Richard Smith.

RICHARD SMITH: You might well have a million dollars worth of reprints, and the profit margin on those is rather substantial. If you don't publish it, then you lose perhaps 800,000 dollars. I mean what could be a more stark conflict of interest?

BOB GARFIELD: So you're sitting in a chilly little room, your legs dangling over the examining table, your symptoms reported and your co-pay paid. And your doctor takes out her prescription pad and orders Synthroid or Paxil or the ulcer drug Omerprazole, and if you're bold enough to ask why Omerprazole, and should she show you what the drug company's sales rep gave her -- say, a glossy reprint from the Journal of Alimentary Pharmacology -- what in the world are you supposed to make of that? The answer is: you don't know. And most likely, neither does she.

BROOKE GLADSTONE: If that catalogue of conflict isn't depressing enough, there's a whole side of the story that didn't quite fit in. That concerns the off-label uses of drugs. That is, drugs prescribed for uses not approved by the FDA. For example, taking aspirin to reduce heart attacks was for some years an off-label use. Companies may not advertise their drugs for uses not approved by the FDA, but of course many drugs are widely prescribed off-label, and the revenue from those sales amounts to billions. So, Bob, this may be tangential to your story, but it's big money, right?

BOB GARFIELD: Yeah, very big money, and not entirely tangential, by the way. Because the media, including medical journals, are at the very heart of the situation.

BROOKE GLADSTONE: Okay. I've performed my function here. Why don't you just go ahead?

BOB GARFIELD: [LAUGHS] Okay. Look, drug companies can't advertise off-label uses. So they have to generate word of mouth and publicity which they do by funding trials and getting the results in journals, and also by cultivating key opinion leaders who hit the hustings at medical symposia to spread the word. For instance, at a recent meeting in Montreal, a key opinion leader paid by Pfizer talked up his study on the effect of the cholesterol drug Lipitor on Alzheimer's patients. Not only did he communicate this to the hundreds of gerontologists at the meeting, he got breathless media coverage about the "exciting news."

BROOKE GLADSTONE: Well, Bob, allow me to play devil's advocate here. If a cholesterol drug slows the advance of Alzheimer's, that is exciting news, right?

BOB GARFIELD: Yeah, if it's true, but who knows if it's true?

BROOKE GLADSTONE: He did a study.

BOB GARFIELD: He did, and this particular study involved a grand total of 63 subjects, and, and you also can't ignore the fact that most key opinion leaders are paid, one way or another, by drug companies. And you just never know how that money affects the needle of anyone's moral compass. Let's take David Pickar, Dr. David Pickar -- he's the former chief of experimental therapeutics at the National Institute of Mental Health and one of the world's pre-eminent researchers on anti-psychotic drugs. He told me that he made so much money as an opinion leader, he could have done it full time -- but he gave it up.

DAVID PICKAR: I don't miss being an opinion leader, because as time - as markets became more competitive, particularly in my therapeutic area, it became more challenging to keep that internal compass going.

BOB GARFIELD: As it happens, Pickar is no longer at NIH. He's founder of his own company, Gabriel Pharma, in the midst of clinical trials on a schizophrenia drug that he developed.

BROOKE GLADSTONE: And so now is he in the market to buy some key opinion-leader buzz for his new drug?

BOB GARFIELD: Well, [LAUGHS] that's exactly the question I asked him, and I have to tell you was quite chilled by the answer he gave me.

DAVID PICKAR: I certainly have been approached by opinion leaders asking if I have sufficient funds for their hire.

BROOKE GLADSTONE: Humph.

BOB GARFIELD: Yeah. Humph. [THEME MUSIC]