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News

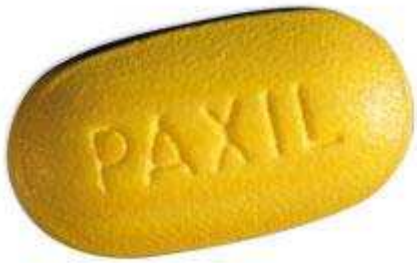
Paxil study under fire

Trial researcher alleges paper exaggerated antidepressant benefits.

Meredith Wadman

The contentious issue of drug-industry influence over medical-research writing erupted on the campus of the University of Pennsylvania in Philadelphia this week. A professor of psychiatry has alleged that several colleagues — including the chair of his department — allowed their names to be added to a manuscript while ceding control to the global pharmaceutical giant GlaxoSmithKline (GSK). The professor, Jay Amsterdam, also claims that the manuscript, written with an unacknowledged contractor paid by GSK, unduly promotes the company's antidepressant drug Paxil (paroxetine), the subject of the study.

"The published manuscript was biased in its conclusions, made unsubstantiated efficacy claims and downplayed the adverse-event profile of Paxil," Amsterdam's lawyer wrote in an 8 July letter to the Office of Research Integrity (ORI), the body responsible for investigating research misconduct in US Public Health Service agencies and its grant recipients.



L. LESSIN/SPL

The letter accuses the study's academic authors of engaging in scientific misconduct by allowing their names to be attached to the manuscript (**C. Nemeroff *et al. Am. J. Psychiatr.* 158, 906–912; 2001**), which has been cited more than 250 times. Documents accompanying Amsterdam's complaint are offered as evidence that "most if not all" of the authors were handpicked by GSK, working in conjunction with the medical-communications company Scientific Therapeutics Information (STI) in Springfield, New Jersey, to lend credibility to a result that Amsterdam says places Paxil in an overly favourable light. In one such document, Karl Rickels, a psychiatrist not involved with the study who looked at the issue for the department in 2001 said that "apparently ... [academic] participants never had a chance to review or even just see the manuscript before it went to press".

"It has always been GSK's policy and practice for the primary author(s) to have final approval on manuscripts," the company says. "The proper use of medical writers serves a legitimate role in facilitating the timely analysis and presentation of clinical-trial data for public consideration."

Amsterdam had recruited patients for the trial but was not included as an author; he protested at the time to his boss, department chair Dwight Evans. Amsterdam was prompted to file his current complaint with the ORI after seeing allegations late last year that Evans had lent his name to an editorial (**D. L. Evans and D. S. *Charney Biol. Psychiatr.* 54, 177–180; 2003**) written by an STI writer who was being paid by GSK (the payment was not acknowledged in the publication). At the

time, the university decided that the allegation of ghostwriting was unfounded.

Amsterdam's charges could prove awkward for the president of the University of Pennsylvania, Amy Gutmann, who is also the chair of US President Barack Obama's bioethics commission. In an 11 July letter to Obama, the Project on Government Oversight (POGO), a watchdog group based in Washington DC that Amsterdam contacted while developing his complaint, called for Gutmann's ousting as chair. The letter takes issue with Gutmann's handling of the earlier ghostwriting allegations. "We do not understand how Dr. Gutmann can be a credible Chair of the Commission when she seems to ignore bioethical problems on her own campus," POGO's executive director, Danielle Brian, wrote.

The university said on 11 July that its School of Medicine will investigate the new allegations. The school's policy, adopted last year, states that medical researchers "are prohibited from allowing their professional presentations of any kind, oral or written, to be ghostwritten by any party, including Industry". The published paper acknowledged that GSK funded the study, but did not note that STI had been employed in the manuscript's preparation, or that three of the co-authors were GSK employees while the study was being conducted. The GSK authors are not included in Amsterdam's complaint.

The five authors whom Amsterdam accuses are Evans, Charles Nemeroff, now chairman of psychiatry at the University of Miami in Florida; Laszlo Gyulai, a psychiatrist at the University of Pennsylvania who has now retired; Gary Sachs, a psychiatrist at Massachusetts General Hospital in Boston; and Charles Bowden, a clinical professor of psychiatry and pharmacology at the University of Texas Health Science Center in San Antonio.

Evans and Gyulai did not respond to interview requests, but the university stated that "both Penn faculty members have been advised of the allegations in the complaint and while they believe them to be unfounded, have made clear to the University that they will fully cooperate with the investigation". Bowden says: "I provided input that was incorporated into the manuscript ... I never had any sense that the manuscript was 'ghostwritten'."

Sachs says he strongly agrees and that he "went physically from Boston to Philadelphia to draft the first draft" with Gyulai. The multi-site clinical trial was conducted in the mid-1990s and funded by GSK (SmithKline Beecham when funding was initiated). It compared Paxil — marketed as Seroxat outside the United States — the firm's new antidepressant, with imipramine, an older, cheaper, antidepressant, and with placebo in treating depression in people with bipolar disorder — a condition with a high suicide risk. Amsterdam alleges that the study: didn't enrol enough patients to come to definitive conclusions; made specious distinctions between subsets of subjects that allowed it to claim a positive result for Paxil in some patients; and played down the side effects of the drug. Nemeroff, the paper's first author, says that the data used withstood rigorous peer review in a process that sent the paper back to the authors for revisions several times. "Right in the abstract under 'results' we report that 'Differences in overall efficacy among the three groups were not statistically significant'," he says. "I don't know how much more straightforward we can be than that."

He adds that "with a 2011 magnifying glass, obviously one would have included in the published paper the use of an editorial assistant". Still, he says: "All [STI] did was

help collate all the different authors' comments and help with references. We wrote the paper."

Paul Root Wolpe, a bioethicist at Emory University in Atlanta, Georgia, who reported to Evans and collaborated with Amsterdam while on the faculty of psychiatry at the University of Pennsylvania, says that the documents imply but do not prove that the manuscript was ghostwritten. But, he says, they indicate "a troubling level of control of pharma over the academic product".

Wolpe adds: "This is not an isolated case, but a systemic problem that needs a coordinated, systemic solution."

CORRECTED: In the original article, Charles Bowden was misidentified as chairman of psychiatry at the University of Texas Health Science Center.

Comments

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#28810

The proper use of medical writers serves a legitimate role in facilitating the timely analysis and presentation of clinical-trial data for public consideration.**performing arts school**
political science school
Psychology degree

Report this comment Posted by: **Jonathan Trott** | 2011-10-28 02:57:09 AM

#39779

I have to admit to being prescribed Seroxat for a period of about 13 months which had to be terminated and replaced with a less harmful substance, I began to feel a sort of anger that I had never before experienced which culminated in feelings of almost unconstrained murderous rage – I actually felt like going on a killing spree – literally. Had I not had psycho-pharm experience I could have shot and killed innocent individuals at random, not all of us are able to recognise and deal with such dangerous drugs.

Report this comment Posted by: **Reb Prole** | 2012-03-02 04:58:04 PM

I know some people taking those pills and they get addicted, once you start, you cannnot stop taking those. There are probably other ways. **#40285**

Alex,
Hot stamp foils

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