

Ethical Problems in the Relationship of Psychiatry to the Pharmaceutical Industry

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Psychiatry and the pharmaceutical industry have been embarrassed by U.S. senate hearings and a series of articles in the New York Times revealing that a number of prominent psychiatrists have failed to report significant financial conflicts of interest. Harvard research psychiatrists, whose work has encouraged the use of antipsychotic medication in children, failed to report to the university most of their consulting income from pharmaceutical companies, skirting a requirement that involvement in human subjects' research be free of significant personal industry remuneration. Another research psychiatrist at Emory University did not declare \$1.2 million of \$2.8 million in industry earnings to his university. An influential psychiatrist who hosted a popular National Public Radio program failed to report \$1.3 million in drug company earnings: when the network learned of this conflict, they removed the program from its satellite service (Harris, 2008a).

The close ties between academic psychiatry and industry that spawned the concerns raised by the U.S. senate hearings have become more prominent since the passage of the Bayh-Dole Act in 1980. The intent of that act was to speed the commercialization of government-funded research discoveries and create new markets and industries. An unintended consequence has been decreased public trust in biomedical research. The conflicts between serving patients and marketing products have led to the formulation by the American Association of Medical Colleges of new standards to restrict the participation of investigators with financial conflicts of interest in human subjects' research. Some observers fear that expanded academic-industry partnerships have led to a credibility crisis for medicine fostered by such practices as increases

in the "off-label" promotion of medication use, industry control of research priorities, bias in reporting research results, the "ghostwriting" of research articles and the involvement of industry in the ongoing education of physicians. (See McHenry and Jureidini in this issue.)

The off-label promotion of pharmaceuticals by key psychiatric opinion leaders has been considered by some observers, including Moncreiff in this issue, to spill over into "disease-mongering" as it seeks to find new uses for approved drugs. An example would be the 40-fold increase in the diagnosis of bipolar disorder in the U.S. between 1994 and 2003 based on the work of the Harvard psychiatrists targeted by the senate hearings. The work of these researchers in identifying bipolar disorder in children has stimulated a greatly expanded use of antipsychotic medications in this age group. More than a quarter of the prescriptions for Johnson and Johnson's antipsychotic, Risperdal, is now for children and adolescents, although only a small fraction of those with a psychotic illness would be expected in this population. The close links between the drug company and the research team is illustrated by the three research goals of the Harvard center for the study of pediatric psychopathology in their 2002 annual report – "improve psychiatric care for children, have high standards and 'move forward the commercial goals of J.&J.'" (Harris, 2008b). A similar concern about "disease-mongering" has been raised by the broad international interest in the "prevention" of psychosis through the use of medications and other interventions before the condition is fully apparent. This interest persists despite the observation that the best screening instruments for the prediction of psychosis have a 98% false-positive rate in the general population

and a 66% false-positive rate in highly selected groups of disturbed young people in two intervention studies funded by the makers of the antipsychotic medications Risperdal and Zyprexa. The use of medications in these prevention trials was associated with a significant risk of side effects (Warner, 2005).

Concern about industry influence in creating bias in the reporting of research results, emphasized by Fava in this issue, has been heightened by a survey which reveals that a majority of medical school research departments do not prohibit the common practices of ghostwriting articles or of industry sponsors inserting their own statistical analyses. Two-thirds of these departments would allow sponsors to prohibit researchers from sharing their data upon conclusion of the study (Mello et al., 2005). Financial conflict of interest has been shown to be frequent, and declaration of this conflict close to zero, among lead authors in medical articles (Krimsky et al., 1998), Diagnostic and Statistical Manual panel members (Cosgrove et al., 2006) and authors of clinical practice guidelines (Choudhry et al., 2002). Selective reporting of research results distorts the data available to practitioners. When published studies of SSRIs were compared to study data submitted to the Swedish drug approval authority, it was found that studies showing positive effects were more likely to be published multiple times and that many articles ignored less favorable data. These biases varied from product to product, making it impossible to form an accurate impression of the effectiveness of any one SSRI (Melander et al., 2003). A review of all the clinical trials in four major psychiatric journals between 2001 and 2003 found that nearly half of the authors reported financial conflict of interest, and that these clinical trials were five times more likely to report a positive result for the test product (Perlis et al., 2006). Pharmaceutical companies hire medical communications companies to write journal articles favorable to their product and pay a well-known academic to publish it under his or her name. At least 10% of medical articles are ghostwritten in this fashion, including 50% of industry-sponsored drug trials (Moffatt & Elliott, 2007).

More than three-quarters of industry spending on marketing is for free samples and detailing physicians. Since samples assist pharmaceutical representatives in getting

appointments with doctors, we may assume that the industry believes that their investment in detailing is productive. The industry hires one representative for every six physicians in the U.S. (See Pollack et al. in this issue.) Teaching hospital physicians meet with representatives once or twice a month on average and, prior to the imposition of recent restrictions, accepted industry funded meals at least once a month (Lurie et al., 1990). Industry also contracts with companies that provide continuing medical education (CME) to physicians. To what extent is the practice of physicians compromised by these efforts? Industry sponsored CME presentations have been shown to preferentially highlight the sponsor's drugs (Wazana, 2000). Meeting with drug representatives, accepting free meals and attending company-sponsored CME events have been shown to be associated with increased prescribing of the sponsor's drugs and non-rational prescribing practices (Lurie et al., 1990; Chren & Landefeld, 1994; Wazana, 2000). Sometimes this marketing is clearly not in the patient's interest. When the anticonvulsant gabapentin was released, the off-label promotion of the drug as a mood-stabilizer for people with bipolar disorder, based on low-quality review articles distributed by industry representatives, led to a surge in its use. The subsequent randomized controlled trials, however, found it to be ineffective for this purpose (Williams et al., 2009). Physicians are at risk of branding themselves as collaborators with the pharmaceutical industry. Although, in a study of resident physicians in Virginia, only a small percentage were willing to wear a pharmaceutical company logo on the breast pocket of their white coat, virtually all were carrying industry-branded equipment, including 95% who were sporting a drug company logo on their stethoscopes – all gifts from company representatives (Sigworth et al., 2001). The physicians' behavior met AMA standards, that industry gifts should be of negligible value, but is that standard adequate? Does carrying company branded equipment constitute product endorsement or, more broadly, an endorsement for the use of medications in general, to the exclusion of other approaches?

A relationship which has been profitable to both pharmaceutical companies and physicians has become an embarrassment. New regulations are being promulgated to restrict gift-taking, funding for educational travel and conflicts of interest in research. Will they be enough to

restore public confidence in the bias-free practice of psychiatry? Equally important, where will psychiatrists learn of advances in psychiatry – from meetings with drug representatives and industry sponsored symposia or from publications that are tainted by selective reporting of industry-sponsored research? Medicine needs the pharmaceutical industry to produce effective treatments and the industry must have a partnership with medicine to be able to conduct human subjects' research on its products. But it is not necessary for the industry to have control over the conduct of the research and its publication. Society should take the opportunity presented by the current crisis of confidence to evaluate whether our present methods of industry funding of medical research and education is in the public interest or whether we should redesign the system so that industry can, instead, contribute to research funding through independent bodies such as the National Institutes of Health.

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