Unhealthy marketing of pharmaceutical products: An international public health concern

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Source: *Journal of Public Health Policy*, May 2016, Vol. 37, No. 2 (May 2016), pp. 149-159

Published by: Palgrave Macmillan Journals

Stable URL: https://www.jstor.org/stable/43948846

Viewpoint

Unhealthy marketing of pharmaceutical products: An international public health concern

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Abstract I consider the current state of pharmaceutical marketing *vis-à-vis* ethical and legal standards and advocate measures to improve it. There is abundant evidence of unethical or illicit marketing. It fuels growing concerns about undue corporate influence over pharmaceutical research, education, and consumption. The most extensive evidence of industry transgressions comes from the United States (US), where whistle-blowers are encouraged by financial rewards to help uncover illicit marketing and fraud. Outside the US increasing evidence of transgressions exists. Recently I have observed a range of new measures to align pharmaceutical marketing practices with ethical and legal standards. In the interest of public health, I highlight the need for additional and more profound reforms to ensure that information about medicines supports quality and resource-efficient care.
Journal of Public Health Policy (2016) 37, 149–159. doi:10.1057/jphp.2016.6; published online 25 February 2016

Keywords: pharmaceutical industry; marketing; promotion; regulation; public health

Introduction

The marketing of medicines is a topic of intense and recurrent debate. While the pharmaceutical industry claims marketing is required for efficient functioning of drug markets,[1] critics accuse companies of using marketing to maximize sales rather than to benefit the health of the public.[2]

Criticism of industry marketing has gained momentum as evidence of illicit marketing schemes accumulates, especially from the United States (US).[3–6] Do commercial marketing schemes undermine the entire edifice of evidence-based medicine?[7,8] Marketing transgressions by manufacturers not only taint the image of both industry and medical practice but

also raise doubt about the ability of regulators to deter illicit behaviors effectively.[9] In efforts to define and then gain control over the situation, state and non-state entities have tried to align commercial practices with ethical and legal standards. These measures often inject a greater complexity into already highly regulated drug marketing.

I consider evidence of unethical and/or illegal sales practices and their implications for public health. I then consider legal, corporate, regulatory, and academic/professional responses. Recent accounts of dubious sales practices, and of proposed counter measures by state and non-state actors, come primarily from the US.[10,11] I also look at marketing and its regulation outside the US. At the end, I conclude by highlighting the need for additional and more profound reforms to ensure that information about medicines supports quality and resource-efficient care.

Pharmaceutical Marketing: A Public Health Concern

Each year the pharmaceutical industry spends an estimated one-third of its sales revenues in marketing.[12] Pharmaceutical marketing is vital to the companies' business model. When it encourages quality and resource-efficient care, drug marketing may benefit prescribers, payers, and consumers of medicines. But does the current business model and the market incentive structure put a premium on rapid expansion of the market? Does it motivate firms to adopt strategies such as encouraging off-label prescribing, overstating the benefits of their drugs, and withholding study results harmful to a drug's commercial profile?[11] If so, such practices are not consistent with the goals of public health – to obtain highly effective and safe therapies at the lowest possible cost.[13]

Given that the business goal of companies is to expand the market, dubious marketing practices would be expected. Public health advocates have called attention to dubious practices for decades, and governments have grappled with this problem using legal and regulatory approaches.[14,15] Despite the long-standing nature of these sales tactics, broader recognition of the problem has taken hold only recently. High-profile US whistle-blower cases have exposed the industry's marketing schemes. From January 2009 through September 2012, the US Department of Justice recovered nearly US$10.5 billion in whistle-blower suits under the False Claims Act, including a record US$3 billion from GlaxoSmithKline for promoting its best-selling antidepressants for

unapproved uses and for failing to report troubling safety data about a top diabetes drug.[16]

Internal industry documents provided by whistle-blowers and made available through subsequent litigation offer unprecedented information to help understand corporate marketing tactics. Steinman and colleagues studied the promotion of gabapentin (Neurontin, Pfizer) by analyzing about 8000 pages of documents made available through litigation.[17] The FDA originally approved the drug in 1993 for epileptic seizures, but gabapentin became widely prescribed off-label for pain syndromes and psychiatric conditions. In 2004, Pfizer's subsidiary Warner-Lambert agreed to plead guilty to charges of illegal off-label promotion. On the basis of analysis of internal company documents, the authors concluded that this marketing of gabapentin was a comprehensive and multifaceted campaign. It included a range of activities from the clearly promotional, such as advertising, to those not typically considered promotional, such as medical education and research.

Others reached similar conclusions about pharmaceutical company efforts to increase sales, often in ways contrary to ethical, regulatory, or legal standards. Companies often blurred the boundaries between clinical trials and corporate marketing efforts. Information gleaned from other whistle-blower suits has become public.[5,9,18,19] These findings fuel concerns about industry bias in medical research and education.[7,20] A growing literature on drug company behavior presents similar concerns.[5,21–28] Scholars discovered many layers of industry bias in the selection, design, publication, and dissemination of clinical studies. Companies had withheld negative study results, misrepresented data, ghost-managed publications, and failed to share clinical data and study protocols with independent researchers.

Lack of access to internal company documents describing sales tactics outside the US has made it more difficult to study marketing practices and misconduct elsewhere, although documents from the US do occasionally reveal offshore sales tactics. In 2012, Eli Lilly and Pfizer both agreed to pay substantial amounts to settle charges of improper payments that their offshore subsidiaries made to foreign officials to win business in Eastern Europe, Brazil, and China.[29,30] In China, for example, to reward them for product sales or prescribing practices, Pfizer employees invited 'high-prescribing doctors' to club-like meetings that included extensive recreation and entertainment.[30]

The House of Commons Select Committee's 2005 investigative report on the undue influence of the pharmaceutical industry in the United Kingdom (UK) also revealed sales tactics outside the US. It referred to "examples cited to us of breaches of advertising regulations, cover-up of negative medicines information, and provision of misleading information to prescribers".[31] A more recent study on violations of the industry's voluntary Code of Conduct in the UK and Sweden has identified discrepancies between the ethical standards adopted by companies and actual industry conduct.[27] Between 2004 and 2012, companies breached their own ethics rules more than once per week on average in each country. Nearly 20 per cent of the violations were 'especially serious', involving transgressions such as pre-license or off-label promotion, or the marketing of prescription drugs directly to patients, both illegal practices in the European Union (EU).

Dubious sales tactics outside the US are a consistent finding in international investigations of the quality of claims made in medical journal advertisements. Claims are often incomplete, inflated, and sometimes clearly misleading.[4,32–34] While ads may be easily screened for transgressions, other sales-promoting activities remain more obscure.

Claims made by industry sales representatives are most likely to influence prescribers as they involve personal contact and often confer special incentives or rewards, but they are also among the hardest to document. Few studies have addressed sales representatives' claims. A study on the information provided by company representatives to physicians in Canada, France, and the US found that company representatives rarely informed physicians about serious adverse events associated with the promoted drugs.[35] Other studies expand on the public health significance of the investigative literature by demonstrating the influence of promotion on physician knowledge and practice, underscoring how misleading and unbalanced claims may adversely affect health by endorsing misuse or overuse of medicines.[26,36–38]

Current Efforts to Govern Pharmaceutical Marketing

The growing evidence – especially from the US – that companies repeatedly and deliberately distorted medical research, information, and appropriate drug use has triggered responses. The US Department of Justice has been particularly vigorous. In line with its litigious tradition, the US government has taken the lead in enforcement actions

against fraudulent practices revealed by whistle-blower allegations. Corporate Integrity Agreements, legal instruments that are by-products of these actions, are government-mandated and require that companies implement and maintain corporate compliance. The US government has used additional legal instruments to deter corporate misconduct and fraud. One recent initiative is the Sunshine Act of 2013 that requires public disclosure of financial transfers and gifts from companies to US physicians.[39]

The pharmaceutical industry has responded to allegations of criminal or unethical behavior by acknowledging a few dubious sales tactics, while continuing to argue that, in the absolute majority of cases, current activities comply with the rules and support quality care.[40,41] Pressured by litigation and public criticism, industry has resorted to developing or updating voluntary codes and guidelines. These include those governing interactions with health professionals, and reporting and sharing of clinical trial data.[41] For industry, voluntary codes and guidelines are key to preventing additional legislation or rules. Yet, in some cases industry trade groups or individual companies have supported government involvement, for example, the Sunshine Act.[39]

On the other hand, the pharmaceutical industry continues to support legal challenges to the FDA's authority to regulate drug promotion. Its representatives argue that a general ban on off-label promotion restricts constitutionally protected 'commercial speech'. The FDA appears to be increasingly open to loosening rules on drug promotion.[42]

Arguably, the key to understanding industry strategy is to recognize the instrumentalist and pragmatic nature of business. Pharmaceutical companies tend to support measures that are most likely to help them achieve their corporate goals. Viewed from this perspective, companies may have good reason to support and even adhere to marketing rules as it helps build trust in the industry and its products, particularly among employees and academic collaborators, as well as among regulators, prescribers, payers, and consumers of medicines.[43] But in many instances, sidestepping the rules has been viewed as a preferable route to commercial success.

Despite fewer examples of illicit practices in Europe, the industry has been under pressure here too.[44] European regulators have felt compelled to grant increased transparency about clinical trial data submitted to them by companies (and about ties between regulatory advisors and industry). The EU has introduced new polices in these areas.[45,46] As in the US,[10] the pharmaceutical industry in Europe has responded to

mounting pressure by updating and developing internal codes and guidelines. In many European countries, as well as in other developed countries such as Canada and Australia, there is a long-standing tradition of self-regulation of promotion.[27] Building on this tradition – and arguably to avoid US-style government intervention – the European industry trade group has developed new guidelines that require companies across Europe to disclose some but not all financial transfers to healthcare professionals.[47] The first disclosures will be made in 2016, but how comprehensive such disclosures will be remains unclear, because publication of information may require consent of the recipient.

Others have reacted to problems created by corporate sales tactics, updating or developing rules that, at least on paper, may prove useful to constrain industry practices. Medical associations and employers (hospitals or universities, for example) have developed professional or employee codes that cover interactions with industry.[48] Medical journals have adopted publication policies to ensure transparency about authors' financial conflicts of interest and to combat ghostwriting.[49]

Measures I describe above do not amount to an exhaustive list of current efforts to regulate or limit the influence of corporate marketing. I have omitted developments in rapidly growing and competitive pharmaceutical markets, most notably China and India,[43] where the problem of industry misconduct may be the greatest.[3]

Beyond Marketing Regulations

Despite efforts to align commercial operations with ethical and legal standards, the ability of initiatives to raise standards of conduct and ensure unbiased medicines information remains uncertain. The prevalence of transgressions and the economic rewards at stake suggest that skepticism is warranted. Although the fines levied in the US may appear astronomical, they may still be too low to deter illicit conduct. Failure to hurt company stock prices plus profits from illicit activities suggests this conclusion.[36,50] Do Corporate Integrity Agreements improve behavior? Not likely, as violations continue despite companies entering into such Agreements.[51]

Criminal investigations and the legal process typically take years, and illicit marketing schemes may continue undeterred.[6] To combat illicit marketing, we need swifter and more efficient regulatory responses in parallel with prosecution. Swift responses may require a more probing

regulatory culture and in the attitude of regulators a shift away from viewing transgressions as a nuisance toward considering them to be a public health threat. The activities of drug companies require meticulous oversight,[52] such as prescreening of promotional material and more active monitoring of promotional information.[27] For countries where there is extensive delegation of regulatory duties to industry self-regulatory bodies, a more probing regulatory culture would seem to require the current balance between self-regulation and government oversight to be reconsidered.[53] Regulatory bodies require sufficient resources to undertake their regulatory duties. Where charges are currently very low (especially outside the US), would much higher fines for transgressions be effective?[27,54]

But even if regulatory bodies had the capacity and the willingness to provide oversight, they face the major challenge of how to acquire knowledge about dubious marketing tactics. This information remains unavailable to those outside the companies, including regulators.[5] In the US, financial incentives for whistle-blowers, plus thorough governmental investigation of allegations, brings out information on corporate activities. Although the US model may not be readily transferrable to countries with different legal systems and traditions, the US success might encourage other countries to facilitate corporate whistle-blowing.[53]

Despite the need to increase the capacity and the willingness of regulators to provide oversight, such initiatives alone are unlikely to raise the standards of conduct and ensure unbiased drug information.[27] Systemic industry bias in clinical research affects the selection, design, and publication of studies and this cannot be altered simply by improving oversight of marketing activities. One crucial step to combat publication and marketing bias would be to require registration and reporting of all clinical trials and sharing of detailed clinical study reports.[55]

From a public health perspective, the problem of pharmaceutical marketing is not limited to fraudulent sales tactics or misleading, selective, or unbalanced claims. Even if companies were to align their sales activities with ethical and legal standards, marketing practices may still adversely influence physician prescribing behavior, contrary to the goals of public health. Marketing always seeks to shift the use of drugs toward newer and typically pricier products, often without therapeutic advantages over older, lower priced drugs.[11]

The Italian Medicines Agency created an attractive model to counter-balance corporate dominance over the creation and dissemination of

medicines information. It required firms to contribute 5 per cent of yearly promotional expenses to fund non-commercial clinical research.[27] Taking that one step further, countries might jointly establish and support financially a network of clinical experts, independent of industry, and task them to conduct key pre- and post-launch trials, educating health professionals and the public by providing unbiased information about treatments.[13] Such efforts would be a radical departure from current clinical research and education, and it would surely be very difficult to realize. Given the public health perils of undue corporate influence over pharmaceutical research, education, and consumption, profound reforms appear imperative.

About the Author

Shai Mulinari, PhD is a multidisciplinary researcher at the Department of Sociology at Lund University in Sweden. His interests include pharmaceutical policy, pharmaceutical industry regulation, and public health.

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