

## BIAS IN DIRECT-TO-CONSUMER ADVERTISING AND ITS EFFECT ON DRUG SAFETY

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### I. INTRODUCTION

Although the Consumers Union is primarily known for *Consumer Reports* magazine, with its expert evaluations of electronic devices, automobiles, and household appliances, we have always been active in the health arena as well, since the magazine was founded in 1936. The monthly newsletter *Consumer Reports on Health* has been around since 1989. More recently, we have established two health-related Web sites. BestBuyDrugs.org was the first and remains free to all comers.<sup>1</sup> Based on the Drug Efficacy Review Project developed in Oregon, it offers consumers what we consider to be the best buys in each of fourteen different drug categories, based not only on efficacy and safety but also on price.

Our other online effort is a joint venture with the *British Medical Journal*, called Consumer Reports Medical Guide.<sup>2</sup> This is an online medical encyclopedia in which we rate treatments for many diseases, primarily on how solid the evidence base is for that treatment.

Here I will address direct-to-consumer (“DTC”) advertising of prescription drugs and its relationship to drug safety. This is a subject that Consumers Union has been interested in for many years. It is a

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1. Consumer Reports Best Buy Drugs: About our Web site, [http://bestbuydrugs.org/aboutus\\_AboutOurWebsite.shtml](http://bestbuydrugs.org/aboutus_AboutOurWebsite.shtml) (last visited Feb. 24, 2007).

2. Consumer Reports Medical Guide: About, <http://www.consumerreports.org/mg/about/about.htm> (last visited Feb. 24, 2007).

virtually unique form of advertising because the consumer to whom it is directed does not control the purchase of the advertised product. The only other commercials of this kind are the breakfast-cereal and junk-food ads that interrupt the cartoons my grandson watches on any Saturday morning. In both instances, an intermediary is necessary—in one case a parent who has the money and, in the other case, a physician who has the prescription pad.

## II. A PLEA TO MANDATE AN INTERMEDIARY IN DTC ADVERTISING

The pharmaceutical industry would have you believe that advertising its products to the public is a good thing and, indeed, it is a very good thing—for the pharmaceutical industry. For every dollar spent on DTC advertising, the industry recoups \$4.20.<sup>3</sup> And last year it spent \$4.22 billion.<sup>4</sup> Just do the math to calculate the take-home bundle: more than the 2005 GDP of fifty countries, according to World Bank data.<sup>5</sup> Add to that another \$7.2 billion spent on direct-to-professional promotion in 2005,<sup>6</sup> and it is no wonder that drug prices are higher here than anywhere else in the world<sup>7</sup>—leading many of our citizens to reach out to Canada and Mexico for their drug supplies, even at the risk of receiving counterfeit material. Others choose to buy food or pay the rent instead of buying medicine.

And invariably, DTC advertising focuses on the newer, more expensive drugs in an effort to achieve market share in the time remaining before the inevitable appearance of “me-too” drugs—drugs that are chemically altered, but basically perform the same function and belong to the same pharmacologic class as the innovator’s drug.

In any normal free-market system, the appearance of competitors will usually drive down the cost in accordance with ordinary principles of supply and demand. Not so in the medical marketplace. The mere fact

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3. MEREDITH B. ROSENTHAL ET AL., DEMAND EFFECTS OF RECENT CHANGES IN PRESCRIPTION DRUG PROMOTION 16 (2003), available at <http://www.kff.org/rxdrugs/6085-index.cfm>.

4. News Release, Nielsen Media Research, U.S. Advertising Spending Rose 4.2% in 2005, Nielsen Monitor-Plus Reports (Mar. 15, 2006), <http://www.nielsenmedia.com/nc/portal/site/Public/> (follow “News” hyperlink; then choose 2005 from drop-down box).

5. See The World Bank, Quick Reference Tables (2005), <http://web.worldbank.org/> (follow “Index” hyperlink; then follow “Quick Reference Tables” hyperlink).

6. U.S. GOV’T ACCOUNTABILITY OFFICE, PRESCRIPTION DRUGS: IMPROVEMENTS NEEDED IN FDA’S OVERSIGHT OF DIRECT-TO CONSUMER ADVERTISING 13 (2006).

7. Dee Mahan, Senior Health Policy Analyst, Dep’t of Health & Human Servs., Statement of Families USA Before the Task Force on Drug Importation (Mar. 19, 2004), available at <http://www.hhs.gov/importtaskforce/session1/familiesUSA.html>.

that there are now five proton pump inhibitors,<sup>8</sup> ten (“SSRI”) antidepressants,<sup>9</sup> fourteen beta-blockers,<sup>10</sup> and ten ACE inhibitors<sup>11</sup> has not led to any substantial reduction in the cost of any one of them as long as their patents hold out. On the contrary, the only marketplace change that takes place is the increase in advertising zeal, where the battle is usually won by the company that mounts the most persuasive campaign, so that the most expensive brand winds up with the largest market share. I once asked a detail person why I should prescribe his company’s product instead of a competitor’s product. His answer: “They pay my salary.”

Cost issues aside, a senior vice president of The Pharmaceutical Research and Manufacturers of America (“PhRMA”) said in August 2006: “The goal of DTC advertising is to provide doctors and patients with accurate educational information about diseases and their treatment options.”<sup>12</sup> Three words in that sentence are worthy of comment: “goal,” “accurate,” and “educational.” I shall examine them one at a time.

The goal of DTC advertising—or any advertising, for that matter—is to sell a product. If that were not the goal, the message would cease to be an ad. There is little doubt that the goal of DTC advertising is to increase the sale of brand-name prescription drugs, and there is also little doubt that the goal is being reached. The main problem is the means by which that end is achieved.

So much for “goal.” How about “accurate”? The medical and consumer literature abounds with examples of inaccuracies and misleading advertising copy in DTC ads. This is an area in which *Consumer Reports* has long been interested. As far back as March 1992, when DTC advertising was in its infancy, we published an article entitled *Miracle Drugs or Media Drugs*.<sup>13</sup> In June 1996, in an article

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8. CONSUMER REPORTS BEST BUY DRUGS, DRUGS TO TREAT HEARTBURN, ULCERS, AND STOMACH ACID REFLUX: THE PROTON PUMP INHIBITORS 2 (2007), [http://www.crbestbuydrugs.org/drugreport\\_DR\\_Prop.shtml](http://www.crbestbuydrugs.org/drugreport_DR_Prop.shtml).

9. CONSUMER REPORTS BEST BUY DRUGS, ANTIDEPRESSANTS 4 (2005), [http://www.crbestbuydrugs.org/drugreport\\_DR\\_Antideprs.shtml](http://www.crbestbuydrugs.org/drugreport_DR_Antideprs.shtml).

10. CONSUMER REPORTS BEST BUY DRUGS, TREATING HIGH BLOOD PRESSURE AND HEART DISEASE: THE BETA-BLOCKERS 3 (2005), [http://www.crbestbuydrugs.org/drugreport\\_DR\\_betablockers.shtml](http://www.crbestbuydrugs.org/drugreport_DR_betablockers.shtml).

11. CONSUMER REPORTS BEST BUY DRUGS, TREATING HIGH BLOOD PRESSURE AND HEART DISEASE: THE ACE INHIBITORS 3 (2005), [http://www.crbestbuydrugs.org/drugreport\\_DR\\_ACEI.shtml](http://www.crbestbuydrugs.org/drugreport_DR_ACEI.shtml).

12. Press Release, PhRMA Senior Vice President Ken Johnson, PhRMA Statement on Direct-to-Consumer Advertising (July 20, 2006), available at [http://www.phrma.org/news\\_room/press\\_releases/phrma\\_statement\\_on\\_direct-to-consumer\\_advertising/](http://www.phrma.org/news_room/press_releases/phrma_statement_on_direct-to-consumer_advertising/).

13. *Miracle Drugs or Media Drugs?*, CONSUMER REP., Mar. 1992, at 142.

entitled *Drug Advertising: Is This Good Medicine?*,<sup>14</sup> we asked panelists in various medical specialties to critique ads culled mostly from the print media. As many as one-third of the ads omitted important information, and only half noted critical side effects in the main text of the message. About forty percent were honest about the efficacy of the product. One of the reviewers volunteered the information that thirty-nine percent of the ads that he reviewed were more harmful than helpful.<sup>15</sup>

A third major *Consumer Reports* article, published in February 2003, just three years ago, entitled, *Free Rein for Drug Ads?*,<sup>16</sup> was based on a computer-assisted analysis of 564 letters from the FDA to various prescription drug makers from 1997 through 2002.<sup>17</sup> Those letters cited false, misleading, or unsubstantiated drug claims; inadequate, incorrect, or inconsistent labeling information; omission or minimization of side effects; unsupported superiority claims; and promotion of off-label uses.<sup>18</sup> And, to make matters worse, a public survey taken at about that time found that half of the respondents believed that drug ads were approved by the FDA before they were foisted on the public, and forty-three percent believed that only fully safe drugs were allowed to advertise.<sup>19</sup> So much for the word “accurate.”

How about the word “educational”? As I mentioned before, that was stated by PhRMA to be the goal of DTC advertising. In fact, one Pfizer vice-president went so far as to propose that such advertising copy be renamed “health information for consumers.”<sup>20</sup> And it is true: The majority of ads do provide the consumer with some information—usually just the right amount to pique enough curiosity to drive a significant minority of patients to their physicians, requesting—indeed, demanding—the selected advertised product.

A recent article by Kimberly Kaphingst and William DeJong found that the concept of a “fair balance” between benefits and risks of television ads was more a promise than a reality.<sup>21</sup> The ads that they scrutinized devoted thirty percent more time in marketing each fact

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14. *Drug Advertising: Is This Good Medicine?*, CONSUMER REP., June 1996, at 62.

15. *Id.*

16. *Free Rein for Drug Ads?*, CONSUMER REP., Feb. 2003, at 33.

17. *See id.* at 35.

18. *See id.* at 33.

19. *Id.*

20. *See* Pat Kelly, *DTC Advertising's Benefits Far Outweigh Its Imperfections*, HEALTH AFF., Apr. 28, 2004, at W4-246, <http://content.healthaffairs.org/cgi/reprint/hlthaff.w4.246v1> (“web exclusive”).

21. Kimberly A. Kaphingst & William DeJong, *The Educational Potential of Direct-to-Consumer Prescription Drug Advertising*, HEALTH AFF., July/Aug. 2004, at 143.

about the benefits than in disclosing each fact about the risks; in other words, the ads “gave consumers about 30 percent less time to absorb facts about risks than about benefits.”<sup>22</sup> They also commented on problems of language comprehension by the consumer, as well as discordant visual images and voice-overs. In other words, the happy faces would remain happy and distract the viewer from the audio when the stern voices spoke about the side effects.<sup>23</sup>

If the intent of DTC advertising were really to educate the public, there would be information about the disease for which the advertised product is used. Informing the prospective patient about the signs and symptoms, the risk factors, and the natural history is certainly part of the educational process. Yet, with the occasional exception of what is loosely known as a “health awareness” ad, it is a rare commercial that calls attention to anything other than the drug. In addition, one almost never sees or hears mention of other options, such as lifestyle changes, that might be better than, or at least as effective as, and certainly less expensive than the drug in question. DTC advertising is not an educational endeavor. Indeed, the very notion that educational material can be incorporated into a drug ad is flawed. Anything that is done to educate the reader has to diffuse the zeal and hype necessary to sell a product. And that would defeat the overall purpose of advertising.

However, educating the public about drugs and disease is necessary and, if properly conducted, can result in healthier and happier lives, but it cannot be left to commercial sources. The responsibility to educate the consumer has to fall to sources that have nothing to sell and are not listed on the stock exchange. That leaves government agencies such as the Centers for Disease Control, the National Library of Medicine, the National Institutes of Health, the Food and Drug Administration, the Agency for Healthcare Research and Quality, certain foundations, and consumer groups.

Well, you might ask, so what if drug ads are neither accurate nor educational? Do they do any harm? The answer to that question is a matter of public record and the Vioxx story is the poster child. The story really started in 1992, six years prior to the approval of Vioxx, when the Prescription Drug User Fee Act (“PDUFA”) was passed by Congress to enable the FDA to speed up the approval process.<sup>24</sup> The result was that the regulator, whose mission is to protect the health of the public, was

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22. *Id.* at 144-45.

23. *Id.*

24. Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491 (codified as amended at 21 U.S.C. § 379g note (2000)).

now being paid by the very industry it regulated. The perception of undue industry influence has been injurious to the FDA. All funding for the FDA should come from public sources and PDUFA should not be renewed. What started out as an \$8.9 million payment in 1993 has escalated to an absurd total of \$232 million in 2004.<sup>25</sup>

In 1998, Celebrex and, six months later, Vioxx were given “priority” status and rushed through the approval process. The cardiovascular side effects that finally led Merck to withdraw Vioxx in 2004 should have been suspected as early as 2000, when the VIGOR trial was reported.<sup>26</sup> Instead, Merck continued its aggressive DTC advertising campaign. Although Vioxx, as a COX-2 inhibitor, was indicated for a relatively small sub-population of arthritis patients with a history of gastrointestinal bleeding or a bleeding tendency, the ads persuaded millions of people to ask their doctors for prescriptions in the misguided belief that Vioxx was somehow more effective than other NSAIDs. That four-year delay may have been responsible for tens of thousands of unnecessary deaths.

More recently, similar problems have come up with selective serotonin reuptake inhibitors. This class of antidepressants may have caused increased thoughts of suicide and, perhaps, an increased number of suicides on initiation of therapy.<sup>27</sup> During the months that the FDA was negotiating a black-box warning with the industry, one would have thought that marketing would have been stopped voluntarily until discussions had been resolved. Not so. And no one really knows, as yet, the number of adverse events that occurred as a result of prescriptions written on demand in response to advertising.

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25. FOOD & DRUG ADMIN., FY 2004 PDUFA FINANCIAL REPORT 4 (2004), available at <http://www.fda.gov/oc/pdufa/finreport2004/>.

26. See Claire Bombardier et al., *Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 NEW ENG. J. MED. 1520 (2000); see also Frank Davidoff et al., Editorial, *Sponsorship, Authorship, and Accountability*, 345 NEW ENG. J. MED. 825, 825 (2001) (explaining that “[m]any clinical trials [are now funded by the pharmaceutical industry and] are performed to facilitate regulatory approval of a device or drug rather than to test a specific novel scientific hypothesis,” and that “[i]nvestigators may have little or no input into trial design, no access to the raw data, and limited participation in data interpretation”). The VIGOR trial was supported by a grant from Merck, and “[t]hree myocardial infarctions, all in the [VIOXX] group, were not included in the data submitted to the *Journal*.” Gregory D. Curfman et al., Editorial, *Expression of Concern*, 353 NEW ENG. J. MED. 2813, 2813 (2005).

27. Yvon D. Lapierre, *Suicidality with Selective Serotonin Reuptake Inhibitors: Valid Claim?*, 28 J. PSYCHIATRY & NEUROSCIENCE 340, 340 (2003) (“The red flags raised by the 1990 clinical reports of increased suicidality associated with treatment with the selective serotonin reuptake inhibitor (SSRI) fluoxetine were followed by anecdotal reports of similar symptoms with other antidepressants of the same class.”).

The reality of such “prescription on demand” was studied by Richard Kravitz and others.<sup>28</sup> In a sting sort of operation, actors simulated patients and feigned symptoms of depression and adaptive behavior disorder and requested prescriptions for Paxil. A large number of physicians acceded and wrote prescriptions for both disorders, even though adaptive behavior disorder does not require drug treatment.<sup>29</sup>

I take issue with the recommendation, in the wise and insightful recent Institute of Medicine critique of the FDA,<sup>30</sup> that the approval process and safety surveillance remain together within the Center for Drug Evaluation and Research. The approval process involves a benefit-to-risk assessment of the evidence submitted with the new-drug application. It is a one-time decision. Post-marketing drug surveillance, on the other hand, is arguably a never-ending process that constantly translates itself into reevaluating that initial benefit-to-risk assessment as new safety issues come up in the post-marketing phase of a drug’s life cycle. And who knows when those issues will arise? After all, Trasyolol, the subject of wide press coverage just recently,<sup>31</sup> has been on the market for thirteen years.

The demand for drug therapy when no drug therapy is warranted is a practice labeled by some as “disease mongering,” defined as “extending the boundaries of treatable illness to expand markets for new products.”<sup>32</sup> The industry refers to these as “health awareness messages.”

We all know that, for many illnesses, especially those for which no tell-tale markers exist, there is a huge gray zone between the normal and the abnormal. Bipolar disease, attention-deficit hyperactivity disorder, restless-legs syndrome, erectile dysfunction, and premenstrual dysphoric disorder are good examples of “diseases” with an assortment of symptoms that many of us can experience from time to time. There are

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28. Richard L. Kravitz et al., *Influence of Patients’ Requests for Direct-to-Consumer Advertised Antidepressants: A Randomized Controlled Trial*, 293 JAMA 1995, 2000 (2005).

29. *See id.*

30. COMM. ON THE ASSESSMENT OF THE U.S. DRUG SAFETY SYS. AND BD. ON POPULATION HEALTH & PUB. HEALTH PRACTICE, *THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC*, at S-7 to S-8 (Alina Baciu et al. eds., 2006).

31. *See Bayer Cancels Trasyolol Clinical Program in Non-CABG Indications*, WORLD DISEASE WKLY., Feb. 27, 2007, at 51.

32. *See* Ray Moynihan et al., *Selling Sickness: The Pharmaceutical Industry and Disease Mongering*, 324 BRIT. MED. J. 886, 886 (2002), available at <http://www.pubmedcentral.nih.gov/tocrender.fcgi?iid=118369> (explaining that “[d]isease mongering can include turning ordinary ailments into medical problems, seeing mild symptoms as serious, treating personal problems as medical, seeing risks as diseases, and framing prevalence estimates to maximise potential markets”).

also now ICD-9-CM codes<sup>33</sup> for shyness and performance jitters. And all are fair game for pharmaceutical hucksterism to persuade people with barely a suggestion of one of those disorders to demand a prescription for the advertised drug. It was no accident that between 1998 and 2002 the largest increase in Viagra use was in men between eighteen and forty-five years of age.<sup>34</sup> Was there an epidemic of potency problems in young and middle-aged men? In fact, when the study results were analyzed, only one in three of those men had a valid indication for the drug.<sup>35</sup>

Between 2001 and 2005 another epidemic occurred—this time insomnia. The number of prescriptions for sleeping pills increased by thirty-two percent during that timeframe.<sup>36</sup> That epidemic coincided with the invasion of three me-too drugs into Ambien's territory, which it had had to itself for seven years. Was *Sleepless in Seattle* that good a movie?

### III. CONCLUSION

If DTC advertising were a drug, it would never have made it through Phase 1 or 2 studies, much less to the point where it would have been worthy of a New Drug Application submission. The reason is obvious: Its risks far outweigh its benefits, which for the most part remain theoretical. But somehow it did get approved and we are left to wrestle with it while the rest of the world—where it does not exist (except for New Zealand)—watches what will happen. To carry the analogy a bit further, any drug that is all risk and is of minimal, if any, benefit deserves to be recalled.

And that is what should happen to DTC advertising; it should be banned. But can that ever happen in this country? The Supreme Court has recently weighed in, in another context, on the applicability of the First Amendment—and upheld the right of commercial free speech. Therefore, short of an outright ban, advertising of drugs to the public should be subject to severe restrictions:

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33. PRACTICE MGMT. INFO. CORP., INTERNATIONAL CLASSIFICATION OF DISEASES (9th rev.), CLINICAL MODIFICATION (6th ed.) (2005). See National Center for Health Statistics, <http://www.cdc.gov/nchs/about/major/dvs/icd9des.htm> (last visited Feb. 25, 2007) (explaining that the ICD-9 is “designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics”).

34. T. Delate et al., *Patterns of Use of Sildenafil Among Commercially Insured Adults in the United States: 1998-2002*, 16 INT'L J. IMPOTENCE RES. 313, 315 (2004).

35. *Id.* at 316.

36. *Sleeping Pills: Are They Worth the Risks?*, CONSUMER REP., Sept. 2006, at 48.



1. A three-year moratorium on all DTC advertising should be placed on all newly approved drugs. During that time, all agreed-upon post-marketing surveillance trials must be completed. Any delay in completion of those trials should result in extension of the advertising prohibition. Any breach of that restriction should result in severe fines and penalties.
2. Advertising copy should be vetted by the FDA *prior* to media release, and strict “fair balance” guidelines observed. Any changes made to the ad after the approval process should be deemed misbranding and result in immediate withdrawal of the ad and the imposition of stiff fines or other penalties.
3. Celebrity endorsement is wholly inappropriate and should be condemned.
4. All ad copy should advise consumers that serious adverse reactions should be reported to their physician and the FDA. The ad should also provide the FDA MedWatch telephone number and Web address.

In sum, the current state of affairs with regard to DTC advertising of prescription drugs is deplorable. The exorbitant millions of dollars spent on this activity is incorporated into the high price of drugs in this country. The main purpose, as with all commercial ads, is to sell a product. Any educational benefit is shrouded in factual inaccuracies, false implications, and unwarranted puffery. And, I believe, such advertising has been harmful to patients. Short of a complete ban, that might not be legally feasible, severe restrictions and limitations should be applied.