

Health Care and the Drug Industry

Part II ~ Patients: Do you feel unmotivated?

Timothy P. Doty, MD Undergraduate, University of British Columbia, Vancouver, Canada

When you wake up in the morning, do you spring out of bed ready to *attack* the day, or are there times when you find it difficult? Do you sometimes feel disinterested or unmotivated at school or work, or as though you may not be reaching your potential? Well don't make any life changing decisions just yet. Researchers have just uncovered important evidence that a certain biochemical imbalance in your brain may in fact be the problem. If you are concerned about your motivation then visit your doctor or the following website for more information.

Reaching out to the public

The previous statement reflects something we are seeing more and more of in the media. While the details of this advertisement or 'public service' announcement are created as an example only, what isn't created is the way in which the information is presented. The approach is common, and whether or not the public realizes it, this announcement represents the first attempt by the drug industry in forming a new relationship with the public. If this advertisement was being aired on a U.S. or New Zealand television station where direct-to-consumer advertising (DTCA) is legal, the above ad would likely list not only the name of the medical condition but also the recently approved drug used to treat the condition. If this were the case you may be asked to "see your doctor and find out if you have Generalized HypoMotivational Disorder (GHMD), or if Motivar is right for you."

The first article in this series demonstrated how both the drug industry and physicians often seek out and foster gift giving relationships on both professional and personal levels. The drug industry devotes a significant amount of time and money to develop partnerships that ultimately influence physicians to prescribe their latest and 'greatest' drugs. However, once they have done all they can with regard to physicians, what else can they do? Like any other business with a product to sell, the drug industry turns to advertising to the public in order to increase its sales. The theory is simple: Once you have done all you can to convince doctors of the need

to prescribe your products, then go straight to the buyers themselves and try as best as you can to convince them of the need to use them.

DTCA: building bridges or building markets?

Proponents of DTCA argue that drug companies are "empowering consumers by educating them about health conditions and possible treatments."¹ It is true that DTCA may inform the public about conditions they may not know about, and it can be useful in motivating people to seek medical help for specific problems they may have. However, it can also lead to the dissemination of biased and misleading information; an increase in health costs from more patient visits and an increase in non-rational prescribing; as well as the over-medicalization of normal human existence.

The messages contained in DTCA are biased mainly because advertising, by its very name, cannot impart information which does not support the product being advertised. Drug companies are in the business of selling drugs and to meet that objective it must show its product in the most positive way possible. Several studies have consistently demonstrated how biased drug companies are when advertising, or 'educating' the public about their products.^{2,3,4,5} Recently, drug researcher Alan Cassels completed a study which looked at Canadian newspaper coverage for the year 2000 of 5 intensely marketed prescription drugs launched between 1996 and 2001. Of the 193 articles that mentioned at least one benefit of the drug, only 32% mentioned a possible side effect or potential harm. Overall, benefits were mentioned nearly 5 times as often as harmful effects. Also, only 38% of the articles listed any quantification of benefits or harms, and a mere 16% mentioned non-drug treatment options.⁶

Because DTCA is so successful at increasing drug sales, individual drug manufacturers have substantially increased their advertising budgets. From 1999 to 2000, the drug manufacturer Merck Frosst upped its DTCA spending by 117.7%. Eli Lilly followed with a mind-blowing 554.9% boost, and Bristol-Myers Squibb increased their DTCA spending by 216.7% during that same time. Overall, industry spending has climbed

from \$791 million in 1996 to a staggering \$2.5 billion in 2001.⁷ Since drug-company expenses are ultimately paid for by patients through the cost of their drugs, these lucrative spending hikes transfer an enormous financial burden to the patient; whether through increased government health dollars, increased out of pocket drug expenses or increased health insurance premiums. Either way patients are the ones who pay the huge cost of advertising.

Proponents of DTCA also profess that advertising allows patients, or rather, 'consumers' to become more responsible for managing their health.¹ There isn't a physician out there that wouldn't agree with the idea that patients are better off when they are able to make more informed choices about their health, and possible treatments for the illnesses that affect them. The problem with DTCA is that not only does it impart information which is biased towards the use of drugs in treating disease as we have seen, but it is also motivated primarily by an approved drug that the manufacturer is trying to market. Thus, when industry claims that a certain medical condition is underdiagnosed and in need of public awareness, they are only doing so because a specific drug they manufacture is available to treat it.

Another problem with DTCA is the subtle shift that it makes from educating the public about a certain disease to creating patient demand for a specific drug to treat that disease. In fact, DTCA has the inherent capacity to make the leap from a list of symptoms to the name of a disorder or condition, *and* the drug used to treat it in as little as 30 seconds. In doing so, the message completely overlooks the fact that many people with the listed symptoms will not have the identified condition. Or even if they do, the mentioned drug may not be the best treatment for them, let alone if a drug is to be used at all. However, once you have introduced a specific drug name into the picture, you are empowering the patient to ask (and often demand) for a treatment which may be completely unsuitable. Despite this reality, the drug industry is quick to pass responsibility over to physicians. "While such advertising prompts more people to seek professional help, it does not dictate the outcome of the physician visit or the kind of help the patient eventually receives."¹ Unfortunately, this comment assumes that physicians are infallible in their attempts to prevent the inappropriate use of prescription drugs. A recent study published in the *Canadian Medical Association Journal (CMAJ)* which looked at the effects of DTCA on prescriptions indicated that more advertising leads to more direct requests for advertised drugs, and more prescriptions for them.⁸ There can be no question that DTCA influences this interaction. The drug industry knows it, and they are capitalizing on it by shamelessly dumping billions of dollars into advertising.

Sending the wrong message

Many of the messages that DTC advertising uses to sell drugs are misleading and outright harmful to overall public health. Many of the techniques that are used to 'educate' the public consist of exploiting insecurities we have about ourselves; fears surrounding ageing, illness and death; and the ever-present socially constructed pressure to be perfect and flawless in appearance, and in whatever we do. These strategies are often enhanced by de-contextualizing the patient from their unique set of life circumstances. In short, the techniques often support ways of thinking about ourselves that medicine should be trying to change. Dr. Joan Meldrum, a Calgary family physician points out her displeasure with an ad for the weight loss drug orlistat (Xenical) which shows alongside a photo of a baby a caption stating: "In the beginning, your weight was in the capable hands of your doctor. It still should be." Dr. Meldrum interprets: "It's saying your weight is not your responsibility, it's your doctors. That's the quick fix. That's wrong." The ad later points out that "your doctor will tell you that losing weight is an important priority because it's a primary cause of diabetes and heart disease." DTC ads often contradict themselves, and this one does so by admitting: "Long-term effects of Xenical on weight-related illness have not been established."⁹ Therefore, DTCA allows patients to be more responsible for their health, but at the same time instructs you to leave everything in the hands of your doctor; and while obesity is known to cause certain life-threatening diseases, it isn't known whether the product advertised will do anything to help reduce that risk.

More recently, Dr. Barbara Mintzes, a health researcher with UBC's Center for Health Services and Policy Research commented on an ad for the oral contraceptive Alesse. The ad shows a picture of a young woman next to a typical birth control packet with a sign that reads: "A lesson in impressions--always leave something to the imagination. Be mysterious." Mintzes says, "It's a bad public health message: take the pill and you can be mysterious. You don't need to discuss birth control with a new partner. She may be protected against pregnancy, but she won't be against sexually transmitted diseases."⁹

Another ad, this one for mirtazapine (Remeron) published in a recent issue of the *CMAJ* shows the silhouette of a couple dancing below a question asking if you're sleepless, anxious, or depressed. Without looking into the context of why this may be so, patients are then assured of having symptom relief in as little as 2 weeks. The problem with this kind of statement is how it transforms and trivializes a potentially serious health situation into a mere inconvenience. Since the ad is from the *CMAJ* it is directed at physicians, and so, at the bottom of the page it states: "Because your

patient doesn't have time to wait."¹⁰ So not only is it reinforcing the notion that people don't have time to be sick, but it also presumes to be telling physicians how to do their job as well. In that statement the ad is really saying: "Excuse me doctor, people lead busy lives so don't bother them with suggestions of anything that might involve time or effort...taking this drug is fast and easy, and that's what your patient wants." Not surprisingly, it's also what the drug industry wants. In a recent executive summary on DTCA, industry claims that increased drug use is actually lowering health costs. "While pharmaceutical treatments have advanced, the price of treating *acute* major depression fell by 25% over 1991-95. This reflects, among other things, increasing the pharmaceutical component, and decreasing the intensity of psychotherapy."¹¹ This statement not only fails to take into account the ongoing costs of treating depression during recurrent episodes, but it also clearly endorses the use of pharmaceuticals over other methods, namely psychotherapy. If anything, treatment options should be focused on using a combined approach, often involving non-pharmacological as well as pharmacological therapies. However, if physicians and patients don't take the time to understand why there is suffering in the first place, one can be sure the patient will end up suffering again. There will be no true healing unless the patient can explore the ways in which their unique circumstances have led to their illness, and relying solely on drugs is like putting a big band-aid on your head; it's a quick fix, not a cure.

Enhancing the doctor-patient relationship?

As patients become increasingly influenced by drug industry marketing efforts, physicians find themselves more and more involved in clinical situations that place their professional responsibility to the patient into conflict with a marketing-inspired consumer demand. If a DTCA inspired increase in patient visits leads to a thorough history, accurate diagnosis, a meaningful discussion regarding pharmacological *and* non-pharmacological treatment options, as well as how the diagnosis fits into the context of the patient's life, then DTCA has served us well. However, if a patient walks in with an agenda that includes confirming their supposed diagnosis and a prescription for a specifically advertised drug, then DTCA is causing more harm than it is good. Current research confirms that DTCA substantially increases the number of patient visits made to physicians,¹² and also shows as many as half of patients would be disappointed if their physician did not fill their request for an advertised drug.¹³ Physicians complain that in an increasingly time constrained practice, DTCA is forcing them to devote increasing amounts of time convincing patients, who are now enlightened health care consumers, of the

inappropriateness of their drug treatment requests,¹⁴ as well as the biases inherent in an industry sponsored advertising campaign. Patients are apt to lose faith in their physicians when advertising messages conflict with professional advice,¹⁵ and if physicians are to protect and enhance the doctor-patient relationship, DTCA leaves them with the difficult task of balancing their professional responsibility to the patient and the sometimes more difficult to ignore concept of customer satisfaction.

If current trends with regard to DTCA continue as they are, patients will ultimately by-pass the physician who refuses to fill the prescription, and order their desired drug more "discreetly" over the internet without having to meet face to face with a doctor. The drive for profit combined with consumers' bent on obtaining the drugs they demand, has prompted a virtual explosion of prescription drug sales over the internet. Now, with some websites, after completing a short questionnaire in which you describe your health situation in thirty words or less, you can greet the FedEx delivery man at your door in the morning with a package containing 3 months supply of anything from Accutane to Zoloft. In one example, a 16 year old from Kansas was able to complete an order for sildenafil (Viagra), sibutramine (Meridia), and Phentermine by placing his actual age of 16 on the order form of an online drug company in the US. Interestingly, one of the reasons listed why patients should order the weight loss drug Phentermine over the internet and not through their local pharmacy and physician is so "you won't have the pharmacist gossiping about you in the local store."

Popular myths about drugs

The drug industry has long supported the increased 'commercialization' of medicine, and unfortunately this has led to the formation and maintenance of several public myths regarding prescription drugs. The first myth is one that is consistent among most other products and technologies: that newer means better. While for many products newer does mean better, with prescription drugs this couldn't be farther from the truth. From 1991 to 1997, a total of 517 new prescription drugs were approved in Canada. Of these, the Patented Medicines and Pricing Review Board determined that only 8.7% represented a breakthrough product, 41.6% of the drugs gave moderate, little or no advantage to those that already existed, and 49.7% of the drugs were 'line extensions' offering a new dosage form or other minor modification.¹⁶ As drug companies compete for 'disease markets' they are constantly seeking approval for their new version of an already approved drug from another company. The activity has actually become so common that the term 'me-too' drug is frequently applied to these products. In 2000, prescriptions for the new ACE inhibitor ramipril rose

among the Ontario elderly population by more than 400% following the release of the Heart Outcomes and Prevention Evaluation (HOPE) study. When this occurred, as well as matching trends in other parts of Canada, McGill University epidemiologists wanted to know why. Their research, published in the *CMAJ* concluded that “the rise in ramipril prescribing was due more to hype than HOPE, as the striking increase was out of proportion to the evidence supporting use of this drug and was mostly due to intense marketing.” In fact, “the marketing was so strong that the unusual rise in monthly prescriptions filled began before publication of the study results in the *New England Journal of Medicine* and *Lancet* in January 2000.”¹⁷

As a society, we have not only come to believe that newer is better, but also if a drug is more expensive it also must be better. The idea that a product's quality is reflected in its price is often wrong and purely misleading when it comes to drugs. Aspirin (ASA) is probably one of the most widely-used, effective, and safest drugs available; at 12¢ per tablet it's also one of the least expensive. The commonly used anti-inflammatory drug Advil (ibuprofen) sells for approximately 15¢ per 200mg tablet, yet its counterpart, Advil Migraine sells for more than twice the price at 33¢ per caplet for the equivalent 200mg dose of ibuprofen.¹⁸ The only difference between the two is that Advil Migraine is solubilized in a capsule, and is ‘designed’ to have a shorter onset of action. One wonders how much of this represents actual measurable and meaningful improvements in migraine treatment outcomes and how much is marketing manipulation?

Another myth could be referred to as the ‘consumer myth,’ and is typified by the hugely supported idea that one needs to buy something in order to ‘get better.’ Industry marketing and advertising continuously bombards the public with messages that link the experience of a runny nose, cough, headache, back pain, upset stomach or feelings of laziness to the purchase of a product. The commercial interest of companies, and our subsequent ease and comfort in using drugs to treat even the common cold are a sure sign of how deeply rooted this myth is in our society. Sometimes a drug is necessary, but it is important that we weigh the options carefully and make decisions based on a need that is realistic, not market induced.

The public ‘on trial’

Throughout all of medical history humans have been used as test subjects. In the 1930's almost 400 African American men were used to demonstrate the effects of syphilis on people. For up to 40 years, doctors gave patients placebos and monitored the effects of the disease, even after penicillin had been discovered. In the 50's US soldiers were given LSD, some of them later suffering permanent memory loss and

hallucinations. When a subsequent lawsuit was brought against the government, the Supreme Court rejected it because the injuries arose directly from activities while in service.¹⁹ While most people would discard the notion that, in the context of modern medicine, this form of testing doesn't take place, there are those who would beg to differ. Doctors and researchers still conduct patient trials, most now on behalf of the drug industry, and many people still suffer the health consequences from these tests. Many patients are already sick, and after exhausting the list of current treatments, they are often desperate to try something else. There are those however, who are not so sick, and their stories cause us to consider whether or not the benefits are worth the risks. In some cases, as with Ellen Roche, a 24 year old technician at the Johns Hopkins Asthma and Allergy Center, the truth about the risks were not known until after she had died. This occurred following an experiment using the chemical irritant hexamethonium to test how some people might develop asthma. Following her death, it was discovered that the literature search of the compound used in the experiment (which only dated back to 1960) failed to uncover earlier evidence of its potential dangers.¹⁹

People are not only being harmed or misled by research and drug trials at the pre-approval stage, but there are significant adverse health effects from drugs that have already been approved. There is often a false notion among the public that once a drug has been cleared by the regulating bodies it is completely safe. A study conducted by researchers at the University of Toronto in 1998 found that between 75,000 and 100,000 people die from normal use of prescription drugs each year in the US. Data from 30 years of hospital records were used, and deaths from overdose or mistakes were not included in the study. It has been suggested that at the same rate, an alarming 10,000 people or more would die each year in Canada from adverse effects of medication use.^{16,20} The drug giant Astra-Zeneca was recently required to pull its prostate cancer drug bicalutamide (Casodex) from the market when it was discovered following a 5-year follow-up study that there was an increased trend towards death in the treated group compared to placebo.²¹ The drugs troglitazone (Rezulin), cisapride (Prepulsid), pemoline (Cylert), and nefazodone (Serzone) have also had similar histories, as have countless others.

Even as we now have the opportunity to learn from past mistakes regarding the use of prescription drugs, many are still being advertised without having been extensively tested in terms of their long-term safety or effectiveness. For example, an ad for the anti-depressant drug mirtazapine (Remeron) indicates: “The effectiveness of Remeron in long-term use (more than 6 weeks) has not been systematically evaluated in controlled clinical trials.”¹⁰ So it hasn't been evaluated

in clinical trials for more than 6 weeks, yet the drug is indicated for depression, an illness which if treated with medication, would require at least several months as a standard therapy to produce optimum effectiveness. There would be no physician willing to prescribe a medication for depression for less than two weeks. So, if the drug has been inadequately tested, then what happens? In this case, the drug company shoulders the responsibility over to physicians by stating in small print: "Therefore, the physician who elects to use Remeron for extended periods should periodically evaluate the long term response of the individual patient to the drug."¹⁰ An ad for the drug venlafaxine (Effexor) also makes a similar statement to physicians, except that its effectiveness "in the long-term treatment of Social Anxiety Disorder, ie. for more than 12 weeks, has not been established."²² Obviously physicians are going to monitor how their patients do on medications, and they certainly don't need the drug industry to remind them of this. However, in these statements there is an implication that it is really up to physicians to conduct the testing; and the patients, whether they realize it or not, are part of the experiment.

Globalization of research and abuse of power

One strategy increasingly used by the drug industry to accumulate the required evidence for their drugs to gain approval is the recruitment of developing nations into their drug trial programs. The ability to test new drugs on large populations in less regulated environments gives the industry immense, and often ethically controversial latitude in how they design and carry out trials. In these countries, the lack of adequate health care often leads to large outbreaks of diseases, and often they are diseases that are only seen sporadically in western nations. When this occurs, the drug industry is quick to use the opportunity to their best advantage.

In 1996 when an outbreak of meningococcal meningitis in Nigeria occurred, Pfizer Pharmaceuticals jumped at the chance to test their new drug trovafloxacin (Trovan), and appealed to the Nigerian government for support. Many physicians near the outbreak questioned the trials ethical standards, claiming "there was no ethical committee at the time of the trial, none met, and no approval was properly given for the trial." Others pointed out that "the 'approval' document was cobbled together long after the experiment concluded and was then backdated." In fact, one of Pfizer's own scientists, Dr. Juan Walterspiel was critical of the trial and warned management about "improper and unsafe" methods before and after the trial. Walterspiel was concerned about treating deathly ill Nigerian children with an experimental drug when an FDA-approved treatment (Rocephin) was available. Trovan was also different as

it relied on oral absorption compared to an injection of Rocephin; therefore any possible effectiveness could be further limited in children whose absorptive capacity was compromised by malnutrition. Pfizer did not share these concerns and Walterspiel was subsequently fired. Trovan was later granted FDA approval, but was then removed from the market in 1999 due to reports of liver failure. All of this occurred *after* net sales of the drug amounted to \$160 million.²³

One wonders what happens when a trial is deemed successful and the manufacturer has been given approval to sell their new drug. How do the people fare afterwards? Do they then get access to the drug? Is the price then made reasonable enough for others to obtain? Most times it is not. In 2003, a group of seriously ill South Korean leukemia patients protested in front of the office of Novartis. After having played a key role in helping Novartis gain record approval for the new drug imatinib (Gleevec), leukemia patients were then left to fend for themselves. At \$19 a tablet, and a year's treatment cost of \$50,000, Novartis left its trial patients in the hands of police, and turned to the more profitable markets in US, Canada, and Europe to sell its new drug.²⁴

Conclusion: motivation for change

The drug industry is very interested in establishing a solid relationship with the public because the public is the ultimate source of its profits. Either through direct payment of drugs with the filling of prescriptions, or indirectly through tax dollars and government sponsored health care plans, or insurance premiums and private health care plans; however you look at it, the public pays for the price of drugs. Advertising has always relied on human fears, instincts, the drive to consume, and the pressure to be constantly productive. For years, advertising has motivated people to rationalize wants into needs, and the drug industry is no exception. We should be very weary indeed when important health information is being made available to the public through advertising, because it is not designed to impart information unless directly related to motivating a product sale.

As patients, we should avoid subscribing to the consumer myth, or the idea that all new medicines represent true benefits over existing ones. Also, the safety of many recently approved drugs has not been clearly established using meaningful long-term studies, and a thorough assessment of these effects are often left up to the physician and patient to determine during longer-term treatment. Because of this, the *Public Citizen Health Research Group* advises people to observe the five-year rule when it comes to prescription drug use. The organization encourages patients to wait "at least five years from the date of marketing to take any new drug unless it is one of those rare

breakthroughs that offers you a documented advantage over older proven drugs.”¹⁶

As previously mentioned, DTCA in Canada is illegal. However, as we might expect, the drug industry strongly supports it, and is therefore continually lobbying for it to be made legal despite the fact that Canadian provinces have stated their continuing opposition to it.²⁵ As evidence of the effects and consequences of DTCA in the United States continues to be studied and observed, the Canadian Medical Association, the Canadian Pharmacists Association, and the Consumers’ Association of Canada have also taken solid stances against its introduction in Canada.²⁵ Instead, these organizations suggest a more practical and beneficial approach would be to use publicly funded alternatives. In this way, public health information that is truly meaningful and important would be provided in an objective and unbiased manner, away from the influence and marketing agenda of the drug industry. As an organization which is primarily accountable to its shareholders and not the patients which it claims to be serving, we can no longer believe what the drug industry says, than we could when the fast-food industry tells us their food is good for us.

Despite the occasional good which comes out of a DTCA-motivated patient visit to their doctor, or request for a specific medication, DTCA clearly does more harm than good. And while the drug industry will employ its greatest statisticians, lawyers and PR teams to try and convince us that DTCA serves the best interests of patients and of the health care system, it will only be doing what is in its best interest. One cannot blame a company for doing what any company would do to ensure it is as profitable as possible. However, when the layers of expressed goodwill and public relations are peeled away, DTCA becomes merely a promotional campaign aimed at marketing their drugs and nothing more.

Our health should not be marketed, discussed in corporate board room meetings or ‘consumerized’ by matching products to disease and illness as advertising would have us believe. Our health should be determined by *real* public need and interest, physicians’ skills, training, and advice, and a government which ultimately supports these two above all else; not by market forces or corporate profits.

Useful Resources

The *Alliance for Human Research Protection*:

- <http://www.researchprotection.org>

The *Women and Health Protection* website:

- <http://www.whp-apsf.ca>

CBC’s *Marketplace* does some excellent investigations on drug trials:

- http://www.cbc.ca/consumers/market/files/health/drug_trials/index2.html

References

1. Holmer, AF. Direct-to-consumer prescription drug advertising builds bridges between patients and physicians. *JAMA*. 1999 Jan 27; 281(4): 380-382.
2. Wade, VA. Mansfield, PR. McDonald, PJ. Drug companies’ evidence to justify advertising. *Lancet*. 1989; 2: 1261-1264.
3. Herxheimer, A. Lundborg, CS. Westerholm, B. Advertisements for medicines in leading medical journals in 18 countries: a 12-month survey of information content and standards. *Int. J Health Serv*. 1993; 23: 161-172.
4. Wilkes, MS. Doblin, BH. Shapiro, MF. Pharmaceutical advertisements in leading medical journals: experts’ assessments. *Ann Intern Med*. 1992; 116: 912-919.
5. Hollon, MF. Direct-to-consumer marketing of prescription drugs: creating consumer demand. *JAMA*. 1999 Jan 27; 281(4): 382-384.
6. Cassels, A. Hughes, MA. Cole, C. Mintzes, B. Lexchin, J. McCormack, JP. Drugs in the news: an analysis of Canadian newspaper coverage of new prescription drugs. *CMAJ*. 2003 Apr 29; 168(9): 1133-1137.
7. National Institute for Health Care Management Foundation. *Prescription drugs and mass media advertising, 2000* [report]. Washington. Available: <http://www.nihcm.org/DTCbrief2001.pdf>. Accessed April 10, 2004.
8. Mintzes, B. Barer, ML. Kravitz, RL. Bassett, K. Lexchin, J. Kazanjian, A. Evanc, RG. Pan, R. Marion, SA. How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DCTA. *CMAJ*. 2003 Sept 2; 169(5): 405-412.
9. McLean, C. The real drug pushers. *The Report*. 2001 Mar 19.
10. Product Monograph. *CMAJ*. 2003 Jan 7; 168(1): 58.
11. Pharmaceutical Research and Manufacturers of America (PhRMA). *DTCA Executive Summary*. Nov. 11, 2002. <http://www.phrma.org/publications/publications//2002-11-11.617.pdf>. Accessed April 1st, 2004.
12. Maguire, P. How direct to consumer advertising is putting the squeeze on physicians. *ACP/ASIM Observer*. 1999; 1-25.
13. Bell, RA. Wilkes, MS. Kravitz, RL. Advertisement-induced prescription drug requests: patients’ anticipated reactions to a physician who refuses. *J Fam Pract*. 1999; 48: 446-452.
14. Huang, AJ. The rise of direct-to-consumer advertising of prescription drugs in the United States. *Medical Student JAMA*. 2000 Nov 1; 284(17); 2240.
15. Perri, M. Shinde, S. Banavali, R. The past, present, and future of direct-to-consumer prescription drug advertising. *Clin Ther*. 1999; 21: 1798-1811.
16. Mintzes, B. How Safe are our medicines? *DES Action Canada and Women and Health Protection*. 2003; 2nd ed. Available at: http://www.whp-apsf.ca/en/documents/how_safe.html. Accessed: April 24, 2004.
17. Pilote, L. Ramipril use in Canada: HOPE or HYPE? *CMAJ*. 2003 Mar 4; 168(5): 568-569.
18. Shopper’s Drug Mart, pharmacy. April 23rd, 2004.
19. Lemonick, MD. Goldstein, A. At your own risk. *Time (Canadian ed)*. 2002 Apr 22; 40-49.
20. <http://www.cbc.ca/stories/2004/04/01/canada/drugs040401>.
21. http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/casodex_prof_e.html
22. Product Monograph. *CMAJ*.
23. Shah, S. Globalization of clinical research by the pharmaceutical industry. *International Journal of Health Services*. 2003; 33(1):29-36.
24. Godrej, D. The great health grab. *New Internationalist*. 2003 Nov; 362: 9-12.
25. Gardner, DM. Mintzes, B. Ostry, A. Direct-to-consumer advertising in Canada: permission by default? *CMAJ*. 2003 Sept 2; 169(5): 425-427.